IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CIVIL NO. 13-CV-4507(CCC)

IN RE: DEPOMED PATENT LITIGATION

TRANSCRIPT OF
PROCEEDINGS
(Public)

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Newark, New Jersey
March 9, 2016

B E F O R E:

THE HONORABLE CLAIRE C. CECCHI,
United States District Judge

Pursuant to Section 753 Title 28 United States Code, the following transcript is certified to be an accurate record as taken stenographically in the above-entitled proceedings.

S/Yvonne Davion
Yvonne Davion, CCR
Official Court Reporter

A P P E A R A N C E S

KEITH MILLER, ESQ.
(Robinson Miller)

MICHAEL SITZMAN, ESQ
CHRISTINE RANNEY, ESQ.
(Gibson, Dunn & Crutcher, LLP)
For Depomed and Janssen

MELISSA CHUDEREWICZ, ESQ.
(Pepper Hamilton, LLP)

LINDA A. WADLER, ESQ.
BASIL J. LEWRIS, ESQ.
(Finnegan, Henderson, Farabow, Garrett & Dunner, LLP)
For Grunenthal

JAMES RICHTER, ESQ.
(Winston & Strawn, LLP)

SAL PATEL, ESQ.
IMRON ALY, ESQ.
(Schiff Hardin, LLP)
For Alkem

KENNETH G. SCHULER, ESQ.
TERRENCE CONNOLLY, ESQ.
(Latham & Watkins, LLP)

AMY M. HANDLER, ESQ.
(Sills Cummis & Gross)
For Roxane Laboratories

SHEILA RAFTERY WIGGINS, ESQ.
VINCENT CAPUANO, PHD ESQ.
ANTHONY FITZPATRICK, ESQ.
(Duane Morris, LLP)
For Actavis Elizabeth, LLC and
Watson Laboratories, Inc

W I T N E S S E S

THE COURT: We are here on In Re: Depomed. It is case Number 13-4507. I will take your appearances in a moment. I want to explain what's been going on in the background because we were supposed to start at 9:30 and of course I'm a little delayed out here.

But, we did receive a consent order with respect to the use codes which we dealt with this morning. And we also incorporated it into the final pretrial order which we wanted to get online before you begin today so it's clear to everyone how we are going to proceed with respect to that. So, we had that done.

In addition, I have canceled my schedule for tomorrow and taken care of that as well. So you will have the full day tomorrow. I understand you have a difficult schedule involving certain witnesses so I wanted to make myself available.

You can probably figure that if you need to sit tomorrow until about 6:30, that should be fine. Will that help at all with these witnesses?

MR. SITZMAN: Your Honor, I think it will. I think we will be able to get everybody in. And we talked about it. I think Friday we'll be able to get all three of the witnesses in without having to go into extra innings.

THE COURT: Perfect. I figure if we stay a little later tomorrow, that should alleviate some of the

pressure for Friday in the late afternoon early evening. That should probably help out a little bit.

So, anyway, that is what I have been tending to. I just wanted to let you all know that we had certain things resolved. But tomorrow the schedule will be, as I said, 9:30 we should be starting at that point.

So let's start with your appearances. We are here today for the first day of trial. Let's start with the plaintiffs.

MR. MILLER: Good morning, your Honor, Keith Miller from the firm of Robinson Miller, Newark, New Jersey on behalf of plaintiff Depomed. With me are my co-counsel from the Gibson Dunn firm Michael Sitzman, Timothy Best and Christine Ranney.

MR. SITZMAN: Good morning, your Honor.

THE COURT: Thanks so much.

THE COURT: Thank you. Good morning.

MR. SITZMAN: Good morning.

MS. CHUDEREWICZ: Good morning, your Honor. Melissa Chuderewicz from Pepper Hamilton on behalf of plaintiff Grunenthal. With me today are co-counsel from the Finnegan law firm Linda Wadler, Bill Lewris and Krista Bianco.

THE COURT: Good morning. Thanks so much.

MS. WIGGINS: Good morning. On behalf of defendants Actavis Elizabeth LLC I'm Sheila Wiggins from Duane

Morris, Newark, New Jersey. With me are co-counsel colleagues Vince Capuano and Anthony Fitzpatrick.

MS. HANDLER: Good morning, your Honor, Amy Handler from Sill Cummis & Gross on behalf of defendant Roxane Labs. With me are my co-counsel from Latham & Watkins, Kenneth Schuler, Terrence Connolly, Lauren Sharkey and Gregory Sobolski.

MR. RICHTER: Good morning, your Honor James Richter; Winston & Strawn on behalf of defendant Alkem Laboratories. And my co-counsel are going to introduce themselves.

THE COURT: Thank you.

MR. ALY: Good morning, Imron Aly from Schiff Hardin.

MR. PATEL: Good morning, your Honor, Sal Patel.

THE COURT: Thank you so much. All right. So, we will begin with openings today. And again I just want to remind all counsel that to the extent any portion of what you're going to discuss is sealed, you are going to let me know so I can take appropriate steps.

But, at this point as we resolved the matter yesterday, the proceeding will remain open unless I hear that something is about to be said that is going to be subject to sealing. And we're all in agreement with that procedure. So just be mindful of it. Thank you.

All right. So we are beginning with the plaintiff and the plaintiff's opening.

MR. SITZMAN: Thank you, your Honor. The reason I approach is do want to be heard on issue first before we begin.

THE COURT: All right.

MR. SITZMAN: Yesterday the Court will recall after what has been a very difficult month of accusations being flown at my firm, myself and my client, that the late a.m. and Watkins firm of Terry Connolly, Ken Schuler and the other attorneys here, had additional evidence to prove that we had committed perjury, contempt and fraud on the Court.

Last night they submitted a letter again accusing us of all of those things. I don't know if the Court has had an opportunity to look at it.

THE COURT: I have not.

MR. SITZMAN: But, what it comes down to is what they accused us of in their papers on Friday which was that attached to my letter, attached to my declaration that was submitted under penalty of perjury that the letter that I attached from their former colleague Alex Long had never been sent to me.

THE COURT: I'm sorry. So the letter that you attached to your submission.

MR. SITZMAN: Correct.

THE COURT: Go ahead.

MR. SITZMAN: That it had never been sent to me. That I had committed perjury, fraud on the Court. And remember my declaration was being submitted in response to their first contention which is we had committed contempt, we were in contempt of the protective order.

The law firm of Latham & Watkins, top rated firm, thousands of lawyers, they say in their letter last night their firm, firmly believes I never received it. They searched their archives, they searched their e-mails.

THE COURT: What is the basis that they received it and what is or what is the basis that you received it? What is their basis that you did not receive it?

MR. SITZMAN: Well, I'm going to show you your Honor. May I approach?

THE COURT: Certainly. Thank you.

MR. SITZMAN: Actually while I'm doing that, your Honor, what I've handed you is two different documents. The first is the e-mail that Alex Long sent to me on Wednesday July 22, 2015 at 8:50 p.m. It says Counsel see below and the attached was the letter dated the same date and attached to my declaration.

Not only did Mr. Long send it to me, but he also sent it to Mr. Chung, Mr. Best and Miss Ranney, all of whom are in the courtroom today. And all of whom would be happy to

come in front of the court and explain that each one of them received this e-mail.

The second document I sent you is the metadata which is and accompanies the e-mail I gave you. And the Court will see filtering through all of that metadata.

THE COURT: There's a lot.

MR. SITZMAN: That every time it hit a server, it went out on the Latham & Watkins server. It came in on the Gibson Dunn server. It went back and forth. There's a handshake that takes place. The dating is consistent all the way through July 22, 2015.

What is their basis for claiming that we committed perjury, fraud, very similar to their allegation that we are also in contempt of court. Very similar to the allegations that Actavis has made. This is about smearing Depomed and us while we enter trial.

For a month now I have been responding to all of these allegations which are baseless. They don't have any basis. They say well we looked at the server and we just don't see you know how Mr. Sitzman got this letter. It was addressed to Bill Baumgartner and Alex Long is no longer here so we are going to submit a letter to the court and tell the Court that what's attached to Mr. Sitzman's declaration is false.

THE COURT: All right. So let me just turn now,

because I do have their submission here which says as to the former let's see Latham has continued its expedited review of its file, can find no evidence that Mr. Long ever sent Mr. Sitzman the July 22, 2015 letter discussed in Paragraph 13 of Mr. Sitzman's declaration and attached as Exhibit 132.

So let's hear a response to that because counsel has presented an e-mail chain and in fact the metadata regarding this particular document.

MR. CONNOLLY: Sure, your Honor.

THE COURT: Thank you.

MR. CONNOLLY: Terrence Connolly for Latham and for Roxane, your Honor.

THE COURT: Thank you.

MR. CONNOLLY: Your Honor, first off if you look at my letter, there is no allegation of perjury, fraud on the Court or anything like that. The allegations that we are engaged in the smear campaign, your Honor, I really hope that you read the letter because it doesn't say that.

THE COURT: Although I'm focusing on very quickly on the correct paragraph that references the fact that you can find no evidence that it was ever actually sent.

Is that the paragraph that we are talking about.

MR. CONNOLLY: In fact we could not find any evidence and this is the first time your Honor you may recall that Mr. Sitzman did attach a copy of a letter, did not attach

this cover note. The letter that was addressed has other counsel. He was not shown as a recipient of the letter. There was nobody from Gibson Dunn shown as recipient of the letter, nor were there any CCs and that's all we had.

I mention Mr. Long has left the firm. So, in the 48 hours that we had to respond, we tried to locate on Mr. Long's e-mail, that were part of Mr. Long's email, any copy of the letter that had indicated that it had gone to the Gibson Dunn firm. Because the accusation here is that by sending the letter to someone who had not yet been admitted pro hoc vice in the case, Mr. Long had waived the confidentiality.

Mr. Schuler was just reminding me that the issue itself about which is contained in the cover letter is confidential. So, your Honor, I will try to avoid getting into the substance of that.

We pointed out in our opposition brief that there was no -- that although Mr. Sitzman had attached a copy of the letter, there was no cover note.

THE COURT: So bringing us up to this point is Mr. Sitzman correct that he was, in fact, sent this letter?

MR. CONNOLLY: Your Honor, I'm not going to contest this. We did not find this. We looked. And to the extent that he has now established, to my satisfaction, that he has, I will withdraw the letter from yesterday, the second part of the letter from yesterday, and I will apologize to Mr.

Sitzman to the extent that he suggested that I accused him of those things.

I don't believe I did, your Honor. I think any fair reading of the letter just pointed out it was an update of our research. We said in a footnote in our brief that we hadn't had the time to complete our search.

We then continued the search in due diligence and then we found, we found and I submitted to the Court this bottom e-mail and that was the attachment that I submitted yesterday which just points out not only was Mr. Sitzman not on the document that he submitted to the Court, we had actually found the cover e-mail transmitting the e-mail which was from Mr. Long's secretary and which listed a host of people but again nobody from Gibson Dunn.

So, as of 11 o'clock the night before last your Honor the only evidence that we had was that there was an absence of documentary evidence that Mr. Sitzman had received it. He had not provided it to you in his opening. So that's why we were digging. We were trying to find out what the basis was.

And at 11 o'clock on the night before last we found the cover note, the lower cover note. We did not see this. I did not know it existed. I felt it important to point out to the Court that we had found it in the subsequent search since I had undertaken to do it in the footnote. And as I

said, I will reiterate, your Honor, I do not contest now based upon this that Mr. Sitzman has received the letter. That is a fact.

To the extent that my letter, I believe, be misconstrued as accusations of perjury and fraud on the Court, etc, I apologize. I don't believe that those accusations are in there, your Honor. I really don't.

THE COURT: I understand where Mr. Sitzman is coming from because it's a sensitive issue with respect to what was actually seen. And obviously the issue, you know, the overarching issue is what was seen and by whom. So I understand how it's been taken.

But obviously at this point we do understand and in fact you do agree that the document was sent, it was sent to Mr. Sitzman, he was accurate with respect to how he referenced the document. And I understand there's a short period of time which to look at these issues. But again they are sensitive issues which is why we are discussing them right now.

MR. CONNOLLY: I agree, your Honor, which is why I apologized. I just don't think that --

THE COURT: Understand.

MR. CONNOLLY: I don't want the record to suggest that I am admitting that did in fact accuse Mr. Sitzman of those things. I don't believe I did. But, to the extent he took it that way, I, for the third time, am apologizing.

THE COURT: I understand, counsel.

MR. SITZMAN: I appreciate the apology and I appreciate that I don't want to beat a dead horse. That's not fair. But, I do want to point out that what has been going on for the last week could have been completely avoided. In fact, all of this should have been avoided and it shouldn't have taken the Court's time. And we shouldn't have been submitting declarations and doing interviews and searching servers and all of these extraneous activities while preparing for trial.

It's time for the merits. We are ready. I shouldn't have to have teams of people looking for e-mails when they could pick up the phone and they could say, in a professional manner, hey, by the way, did you get this e-mail? If you've got the e-mail, could you send it over.

I talked to Ken Schuler twice yesterday, twice yesterday before they submitted this letter. Hey, Mike, we're about to send a letter to the court and we're going to tell them that the letter that you attached to your declaration under penalty of perjury was not in fact delivered to you.

THE COURT: Again I fully respect where you're coming from and I understand the issue is a little bit heated. And I am sure everyone is trying to put their strongest position forward if they believed that you hadn't received the letter, I think that was the impetus for sending that in. Was it correct? No. It wasn't correct. And I think at this point

counsel has indicated you've fully established that you received the letter.

And to the extent there was any implication he was saying anything beyond that in his letter, he hopes you understand that he wasn't.

Is that an accurate recitation.

MR. CONNOLLY: Yes, your Honor. I think that was pretty clear.

MR. SITZMAN: And I accept the apology. I really appreciate that. I would like to see this sort of come to an end. We've got a long trial ahead of us.

THE COURT: I agree.

MR. SITZMAN: We have a lot of work to do.

THE COURT: And we do still have some issues out there. And perhaps if we are able to work together, they might be more quickly dealt with. I understand that as far as the issue that's pending with respect to these letters I'm not going to go into them in detail right now. Obviously because we are hoping to do our openings right now.

But, when we get together to discuss those I'm going to set a specific date and time at the end of the day when we can do that, not today, but for another day. I'm hoping that we will be able to address that in a spirit of cooperation as well and get beyond this. All right.

Anything else on this particular issue? Counsel.

MR. CONNOLLY: Not from me your Honor.

THE COURT: Anything else?

MR. SITZMAN: The only thing I would like those two documents I guess entered or if the Court wants me to separately since the letter has come in and it has been put on the docket, I would like those two documents put on the docket as well.

THE COURT: Do you want to do a cover letter or we could certainly just put them on the docket but then they have no reference point.

During the break if someone wants to do a cover letter you can show it to counsel, e-mail it to us, then we would be happy to assist to put it on the docket today.

Is there any issue?

MR. CONNOLLY: I'm going to ask Mr. Sitzman to check whether his declaration, the original declaration is on the docket because I believe some of those original papers were not actually filed on the docket. So if it's on the docket, then you can cure it. But, if it's not on the docket, I don't think there's anything --

MR. SITZMAN: The redacted version is filed under seal on the docket.

MR. CONNOLLY: By the way, these papers were also filed under seal.

MR. SITZMAN: Right.

THE COURT: But these documents you are not looking to have them filed under seal? Do you want to consider that?

MR. SITZMAN: I don't think they have any confidential information.

THE COURT: I'm not certain. You can look at your metadata and see if there is. Do you want to take a look at the docket?

MR. CONNOLLY: As long as the attachment isn't.

MR. SITZMAN: The letter is not attached. It's just those two documents.

MR. CONNOLLY: These two documents do not contain any confidential information.

THE COURT: I'm sorry, what was the last --

MR. CONNOLLY: These two documents that Mr. Sitzman just handed me do not contain any confidential information.

THE COURT: During the break if you want to have someone on your team draft a letter or during lunch, that's fine, a cover letter. You can send it to us and we would be happy then to assist by putting it on to the docket. All right.

Okay. Any other matters before we start today? Anything else? Is everyone's computer equipment working properly? Any issues? We are closing the skylight. Hopefully

that should aid with viewing the screen.

MR. SITZMAN: Your Honor, may I approach?

THE COURT: Yes, certainly.

MR. SITZMAN: Your Honor, what I handed up is a set of demonstrative exhibits that I'm going to use during the course of my opening.

The other quick question before I begin, would the Court mind if I approached the screen from time to time to point a few things out?

THE COURT: That is totally fine. And with respect to the slides, has everyone on the defense side taken a look and has a copy? Yes.

MR. ALY: We just received a copy.

THE COURT: I gather at this point no issues. Any issues so far? If you want to take a moment. Any issues?

MR. SCHULER: I think it comes to about 49.

MR. SITZMAN: There's going to be a need to change the configuration.

THE COURT: Page 49.

MR. SCHULER: Slide 49.

THE COURT: I flag it at Page 49 but if you would like to give me a reminder before you get to that point.

Are we in agreement it's Page 49 where we start?

MR. SITZMAN: We will stop at 48, pause.

THE COURT: Fine. Because just what I indicated,

if you would like to give me some lead notice even though I have stickered it so we can take care of that. All right.

Any other issues? Anything else? No? Okay. So let's begin with the opening on behalf of plaintiff.

MR. SITZMAN: Thank you, your Honor.

THE COURT: Thank you.

MR. SITZMAN: Thank you and I thank the Court staff, by the way, for persevering with us. You have met most of the team here and we are happy to be here. Let me also introduce Mr. Paul Simboli (ph) who is in the courtroom from Depomed.

THE COURT: Hello, sir, how are you?

MR. SIMBOLI: Very well. Thank you.

MR. SITZMAN: Vice-president assistant general counsel. And also in the courtroom who will be testifying later is the vice-president of finance from Depomed Jack Anders.

THE COURT: And Mr. Anders. Hello Mr. Anders. How are you?

MR. ANDERS: Good.

THE COURT: Good.

MR. SITZMAN: Let me begin by giving the Court just a brief roadmap as to where I'm going on my opening. First I want to talk about, give the Court some background on the science and treatment of pain that's relevant to this case,

some of which we've touched on. But, I want to go into a little bit more detail today.

Next I want to talk about the inventions, then the patents and then the issues that will be the subject matter of the trial, defendant's infringement, and then the validity of the patents.

So let's start with treatment and pain. As I told the Court in December, there are two types of pain that are relevant to this case, nociceptive pain and neuropathic pain. Nociceptive pain are what everybody calls a noxious stimulus. This the type of pain where you stub your toe, you twist your ankle, you unfortunately hit your thumb with the hammer as depicted there. That's the type of nociceptive pain we are talking about.

THE COURT: Would you also refer to it as external or could it be internal but caused by an injury?

MR. SITZMAN: It could be internal as long as it was caused by some --

THE COURT: Pressure?

MR. SITZMAN: Pressure. Well, pressure or some single point that when removed, that's the key, when removed, the signal goes away.

THE COURT: Okay.

MR. SITZMAN: Let me contrast that with nociceptive pain. What happen is the nerves become damaged,

they become not functional and are not operating correctly. They are constantly sending signals, wrong signals of pain through the body, different parts of the body and different control centers.

And as you can see in terms of the contrast, there's no stimulus or isolated or identifiable stimulus that's causing it. It's the actual nerves themselves that are suffering from that pain.

Now, in order to feel pain, pain signals have to make their way to the brain. And they do that through the ascending pathways. The brain has to perceive the actual pain.

The descending pathways, the ones coming down from the brain, that's what's implicated in the neuropathic pain aspect. It's the descending. And that's shown here, the descending pathways. That's what's implicated on the neuropathic side of the chart.

The neuropathic pain communication is dependent, in part, on what we call neurotransmitters. And neurotransmitters are those chemicals that transmit a signal from one nerve or neuron to another. And examples of neurotransmitters that you're going to hear in this case and you will hear also there are things like Dopamine serotonin 5 HT Epinephrine, neuro epinephrine, those are all the chemicals that are in that what we call that synaptic space that delivered the signal from one nerve to the next.

Now, opioids which you've heard a lot about already --

THE COURT: I have.

MR. SITZMAN: -- they play a very important role, as you can imagine, in reducing pain signals. And they do that by interacting with the opioid receptors on individual nerves.

Now there's a host of different types of opioid receptors. Each one has its own characteristic. Each one also relates to a different source of communication.

There are three primary sources of opioid receptors, MU, Kappa, delta. And then you can see from that chart, which you don't have to memorize, that they are, within each class, there's multiple sub types. So you have MU 1, 2, Kappa one. And it's the targeting of these specific receptors with particular opioids that can bring about certain pain relief.

THE COURT: I know in your brief you talk a lot about the MU opioid. You are going to focus on that today?

MR. SITZMAN: Exactly. Exactly.

THE COURT: Okay.

MR. SITZMAN: So it's the selective binding of the opioids to these receptors, the MU opoid with regard to this particular medication that reduces that pain signal that's headed to the brain.

Now, opioids are activated by opiates. That's

how they got their name. The oldest known form of opioids is opium. That's how this all comes together.

Today in the modern world we've got the drugs we are going to talk about. I tried to stay away from them on this slide. Morphine is one of the big daddies of opioids. It has problems. It has side effects. Things that the Court, I'm sure, is aware of in public. OxyContin is another one.

All right. Let's turn briefly now, well, or longly, to the inventions. The inventions start out at Grunenthal. Grunenthal is a privately-owned pharmaceutical company in Aachen, Germany. Since the early 1960s, Grunenthal has been investigating and developing analgesics compounds. One of its first successful analgesics was Tramadol.

Tramadol was first synthesized in 1962. Tramadol is what we call a centrally acting opioid analgesic. Centrally acting in that it acts on the nerves in the central nervous system, the brain and spine, primarily the spine.

Now Tramadol is a fairly complex mixture. Tramadol is administered as a racemic mixture. Up above you will see 1R, 2R, 1S, 2S Tramadol. It exists in two enantiomers. When you take a pill, you are getting both enantiomers. When it hits the body, it then becomes metabolized into two more molecules, 1R, 2R, 1S, 2S O desmethyl.

Now each of these chemicals has its own complex,

I'm sorry, each form has its own pretrial. It's the combination. In fact, you need the combination of all of these molecules to bring about the analgesic activity of Tramadol. That's what they indicated in the middle. That's the new opioid activity, the serotonin reuptake inhibition and NE is shorthand for neuro Epinephrine uptake inhibition. Tramadol has some shortcuts.

THE COURT: So, back to that, though, you need the full racemic mixture. You need both the enantiomers in that pill and then they breakdown into those two substances.

MR. SITZMAN: Exactly. You cannot identify any one of them as controlling one activity or one mechanism of action. In order to bring about the full analgesic effect of Tramadol, you have to have the racemic mixture. The racemic mixture has to undergo metabolism. The metabolites have to work.

I think I was talking about some of the shortcomings of Tramadol. It's relatively a weak opioid. The gold standard here is Morphium which is very strong. And like I said, has its own drawbacks in terms of side effects and in terms of harm and danger. But Tramadol is relatively a weak opiod on the scale of opioids.

THE COURT: So in terms of what you would prescribe it for, what would be the type of things you would use Tramadol for? It sounds like it's not really as strong as

some of the other drugs. So what would you be using it for?

MR. SITZMAN: You would use it for nociceptive acute pain, for example. By the way, just because it's considered a weak opioid, doesn't mean that it doesn't have utility or analgesic properties.

There's some people that cannot tolerate morphine or some of the more potent opioid drugs. So Tramadol is a good substitute for that.

THE COURT: So, what types of things would you -- I mean in terms of level of pain, would you be prescribing this --

MR. SITZMAN: I would like to reserve most of that for the clinical experts that are going to be here. But, to give the --

THE COURT: I am just trying to gauge its relative strength.

MR. SITZMAN: Relative to morphine?

THE COURT: Yes.

MR. SITZMAN: Again it would depend. And I don't think I have enough clinical experience to give you kind of numbers of days and dosages that I would give a particular patient.

THE COURT: Fair enough.

MR. SITZMAN: But, the way I look at Tramadol, the way we view Tramadol is it is very helpful in treating that

short term acute pain that you get, that nociceptive type pain where you don't need to treat other conditions, other pains. And you know that this is going to be perhaps a short lived pain. Again, I'm going to defer to the medical experts on that.

It's also a complex molecule mixture, that it's got the racemic mixture in those metabolites. Given the indication and the continued need to find pain treatments with greater efficacy and less side effects.

THE COURT: What were the side effects for Tramadol?

MR. SITZMAN: One of the biggest, for example, is constipation. And that's not uncommon with opioids. But that's one of the biggies. Other gastrointestinal problems are also associated with Tramadol. That's not to say that everything else is free of those. But, these side effects are in existence. And there is this long felt need to find drugs that can deliver an effective dose of opioid that's efficacious and have less of these side effects.

So, against this backdrop, Grunenthal decided to look for some new successor. And while it could have started anywhere in the field of pain treatment, Grunenthal decided to start and focus on systematically varying the control structure of Tramadol in order to find some new successor compound.

Grunenthal identified three structural features

within Tramadol that it felt were very important. First that it had an aromatic ring. Second, that it had a tertiary amino or nitrogen atom. And by the way that's A B and C I might come back and refer to them as A B C.

THE COURT: That's fine. A is an aromatic ring and so on I'm with you.

MR. SITZMAN: And C the cyclohexane ring. This ring structure here locks this molecule together. It holds A and B in just the right confirmational position in order to bind to the MU opioid receptors and other receptors within the body. It holds it in that perfect space.

That's why this ring structure was important to hold this all together and keep this molecule rigid because they knew it worked.

So, in order to make sure you had an new drug that would hit the same receptors, you gotta have the same confirmation or at least try.

For ten years Grunenthal worked on trying to find a successor to Tramadol, but to no avail. Could not identify a viable candidate. They tested approximately 550 compounds, the evidence will show . The desired profile for the new drug that Grunenthal had set out was very demanding. And many people at Grunenthal, especially after ten years of working on this, felt that there was no real prospect of success.

In scientific terms, Grunenthal was stuck. That

is until May of 1992. In May of 1992 Dr. Helmut Buschmann comes to Grunenthal. The Court will hear from Dr. Buschmann later today. Dr. Buschmann was skilled and trained in medicinal and synthetic chemistry. And when he came to Grunenthal, no surprise, he was assigned to the successor project and brought up to speed as to what Grunenthal had been doing for the last ten years in terms of synthesizing new compounds.

Dr. Buschmann, you will hear, started synthesizing compounds just like the rest of the scientists at Grunenthal. Nothing truly remarkable about any one compound until Dr. Buschmann decided to take Grunenthal in a completely different direction.

Remember the figure I just showed you. Dr. Buschmann proposed opening or breaking the cyclohexane ring. That was a radical departure. Dr. Buschmann felt that if they lost some rigidity for some reason, he believed he might be able to come up with a new compound.

Now, this flew in the face of everything that not only Grunenthal knew, but that the scientific community knew. Losing rigidity to obtain and try and keep that confirmational configuration within the molecule didn't make sense. All of a sudden you are going to now make this floppy molecule that can move and change into all kinds of shapes.

Additionally Dr. Buschmann wanted to do a few

other things. He wanted to remove the C-1 hydroxyl group and he also wanted to modify that aromatic ring that you see in A.

THE COURT: So you are saying it would be counterintuitive at that time to have come up with a linear structure?

MR. SITZMAN: It's as if you read my opening statement. Exactly. That's exactly right. And it wasn't that easy, by the way. It was counterintuitive not only to the people at Grunenthal who had been working on this for ten years but to the scientific community at large.

The Court's going to hear from Dr. Bill Roush who is an expert in synthetic chemistry and medicinal chemistry. And he is going to talk about what was expected and known for a person of ordinary skill in the art in 1994 and explain how far outside the box this approach was.

THE COURT: Were any of the other analgesics at the time in a linear structure?

MR. SITZMAN: No.

THE COURT: There were none?

MR. SITZMAN: Well, so, I'll keep moving forward.

THE COURT: I'm sure it's coming in somewhere. Go ahead.

MR. SITZMAN: So, you can imagine, by the way, how Grunenthal reacted to Dr. Buschmann wanting to do this. And they resisted. Dr. Buschmann's going to explain that they

resisted. They he had to fight with his personnel in order to make these linear compounds. Ultimately Dr. Buschmann said that he would continue and he agreed he would continue making the cyclical compounds only if he could try some of his linear compounds.

Grunenthal was not going to give up on its teachings, its knowledge and the idea that cyclical compounds were the way to go.

To make that situation, by the way, worse for Dr. Buschmann, the chemical synthesis group, the group that he was in, was receiving incredible pressure from the executives at Grunenthal that the entire project was going to be scrapped. If they could not find a rational candidate to move forward with, they were going to scrap it.

Because at that point in time it was 12 years of work. They had spent millions of dollars and 12 years of time and they didn't have -- they had lots of possibilities. They didn't have a rational candidate to really move forward with.

Dr. Strassberger, I was going to tell you about Dr. Strassberger, he's the director of computational chemistry. And he said at that moment in time that finding a candidate with all of the required characteristics in a single compound, could not be done. Dr. Buschmann pushed forward. And by 1994, Dr. Buschmann's laboratory produced, synthesized more than 300 compounds, both cyclical, because as I was telling you he had

to continue that cyclical approach, and linear. The linear compounds were unlike anything that Grunenthal had ever seen or any of its competitors.

Your Honor was asking about what the competition was doing. You are going to hear from Dr. Buschmann about what the competitors were doing, and none of them were at this point.

Many of the linear compounds Dr. Buschmann sent to Dr. Elmar Friderichs who tested these linear compounds in a nociceptive animal model. They wanted to see whether any of these linear compounds would work. And lo and behold all of the linear compounds that Dr. Friderichs had received showed analgesic activity.

The data was very well received at Grunenthal. But, they still weren't convinced and they moved forward in drug development with several linear compounds but also a couple of the cyclical compounds as well.

In December 1997, three years after synthesizing Tapentadol, it was selected as the lead candidate that Grunenthal would move forward with.

Dr.Buschmann and his co-inventors filed for patent protection for this novel class of linear compounds. That led to the issuance of the '737 patent. Let me just pause here for a moment. The court knows that the patent at issue is a reissue patent that we refer to as the '593. This is the

original patent that gets reissued as the '593.

THE COURT: Going back to Elmar Friderichs.

MR. SITZMAN: Yes.

THE COURT: When the substance was sent to him, tell me again what he did with it.

MR. SITZMAN: He used --

THE COURT: He tested it?

MR. SITZMAN: He tested it in an animal model, that's an in vivo, to see if it had any analgesic activity.

THE COURT: Prior to that, had it been tested in animal models?

MR. SITZMAN: The linear compounds? No.

THE COURT: That was the first time?

MR. SITZMAN: That was kind of that first test.

THE COURT: Okay.

MR. SITZMAN: So, I don't want to lose this point. If the Court hears '737 or '593, we are talking about either the reissue or the original patent, but it's that same composition of matter invention.

As a drug candidate, Tapentadol was a significant departure, as you can imagine, for Grunenthal from what it was used to. Remember my discussion of Tramadol just a few minutes ago which was racemic mixture, two enantiomers, metabolites. Tapentadol, on the other hand, is just the minus enantiomer and a single molecule.

Tapentadol only had two methods of action. It had that MU opioid receptor activity. It had the neuro epinephrine reuptake inhibition but it didn't exhibit that serotonin reuptake inhibition that Tramadol had.

So, by going with Tapentadol, Grunenthal went from three methods of action to two mechanisms, sorry, mechanisms. The bottom line and the take away here is that identifying synthesizing and developing Tapentadol was a huge leap of faith by Grunenthal.

While we're on Grunenthal, let me just talk basically about the internal structure without much detail. But it's an internal structure to keep in mind how things worked at Grunenthal.

The process of going from synthetic chemistry to production. Here in synthetic chemistry this is where Dr. Buschmann was, along with other scientists. And the focus here is identifying new novel compounds. This is in that space. What they're looking at is they're looking at generating new compounds. They are not working on quantities, they are looking for new and novel compounds. They are producing very small amounts of these products in fact.

And this is where the synthesis of example 25, for example, took place. After synthetic chemistry, though, the product, the project, the compound then makes its way through chemical process and development. Now here the focus changes

because we are no longer looking at developing new compounds. Here what we're looking at is some efficiencies and savings on some opportunities to start thinking about some scale up and generating a little bit more for more testing, more in vivo testing, more invitro testing, more analgesics to analyze the compound certainly with much more quantities than they had in synthetic chemistry.

When it eventually makes it way to production, the focus again changes again. Now we're looking at large scale scale up. Producing enough compound in the most efficient way so that the dosage form can be made in an economical way for delivery to the patient.

Each time this compound or the project or the particular compound at issue moves along this process, the process changes, the focus changes, the process changes. They are still making Tapentadol or they are still making whatever the drug is at issue. But, the process changes for making it.

Now I'm going to come back to this in a few minutes but I just wanted to layout that structure at this point.

THE COURT: Okay.

MR. SITZMAN: We've been talking about Tapentadol and the Tapentadol molecule. Let's talk a little bit about what happens when all the Tapentadol molecules are packed together. This brings up the concept of polymorphism.

Now, generally speaking, polymorph is the ability of a solid material to exist in more than one form or crystal structure. This is a classic example of graphite and diamond. Two different crystal structures. Same chemicals, two different crystal structures.

Now crystalline solids can exist in one of seven different forms. Here's the seven different crystal structures. Now each one has different properties. But, by and large all the crystals fit into one of these basic structures.

Now, up until the late 1990s Grunenthal was not focusing on polymorphism. Dr. Buschmann tried to convince Grunenthal that solid state analysis, analysis of these forms of crystals of the actual solid form of the compound, that that was important. But Grunenthal did not have, at that time, a solid state laboratory.

So, Dr. Buschmann convinced Grunenthal to go out and hire its first inorganic chemist. Normally in the synthetic chemist group you've got all organic chemists. Now Grunenthal is going out and it's going to hire its first inorganic chemist to study crystal structures.

And in 2000 Dr. Michael Gruss who the Court will hear from in the next day or so was hired in 2000. And he came to Grunenthal as the first inorganic chemist to work on and develop a solid state lab.

Shortly after Dr. Gruss arrived at Grunenthal he started to collect various Tapentadol samples from all over Grunenthal. He was asked to take a look at what Tapentadol is, what the structure is. And he was studying Tapentadol as well as other compounds that they were all interested in.

Since Grunenthal at that time didn't have the XRPD type machinery, in fact they hadn't even bought one yet, Dr. Gruss sent the samples out, that he had, out to outside labs and asked for XRPD patterns of all of them to come back.

When they came back, Dr. Gruss reviewed all the patterns and he concluded, after looking through and analyzing all of this XRPD data, along with some other data, by the way, it was on DSC data, there was some other data on the Tapentadol molecule that was available to him, but from all of that data he was able to conclude that there were two forms of Tapentadol. Form A, which is the monoclinic crystal and form B which is the ortho rhombic crystal.

Now, many of the samples that Dr. Gruss received back were form A or mixtures of form A and B. But, in 2002, in early 2002, Dr. Gruss saw the XRPD pattern of batch 0 which was the original batch of Tapentadol that Dr. Buschmann synthesized in his laboratory eight years earlier in 1994.

This is the XRPD pattern of batch 0 showing that its form B and there is no form A present. And again that was done eight years after the fact.

After seeing this, Grunenthal wanted to confirm this result.

THE COURT: And what would it look like if there was form A present?

MR. SITZMAN: You would see A peaks here at various different points. Remember the patent, the '364 patent identifies certain particular peaks in terms of claim one and claim two. It identifies some of those two theta peaks that are specific to form A. And Dr. Joel Bernstein is going to be here in a week or so.

THE COURT: And explain what it would look like and why this looks like a perfect form B?

MR. SITZMAN: Exactly.

THE COURT: And this one, this particular exhibit is 1994?

MR. SITZMAN: No, it was done in 2002.

THE COURT: 2002.

MR. SITZMAN: The results came back in 2002.

THE COURT: But this is the exact batch from 0.

MR. SITZMAN: Yep. This is batch 0. This is what, this is the first manufacture and synthesis of Tapentadol. The very first.

THE COURT: Okay.

MR. SITZMAN: Now, seeing these results, Grunenthal wanted to confirm what it was seeing. So, it asked

Marita Mueller, who you've heard a little bit about --

THE COURT: I certainly have.

MR. SITZMAN: -- to try and do and perform and resynthesize example 25, to go back and resynthesize and she did. She did it twice. And what she found when she did it was example 25 yielded form B.

So, what do we know of batch 0 form B carrying out example 25, form B? But, we have other results from across the company that Dr. Gruss has received samples back in XRPD patterns showing there's form A form B, even mixtures of form A.

THE COURT: Going back to Marita Mueller for a moment, I know we discussed this on some of the motions leading up to trial in terms of her performing this analysis. I think she did it twice. She got form B twice. We had addressed at the time what she had started with and how she got there. If you could go through that again.

MR. SITZMAN: I will. Let me, I will preview where I'm going to be. She started at the beginning of example 25 and faithfully carried out example 25 from start to finish . And she did it twice.

THE COURT: And you will go through that again as we get to another point on this.

MR. SITZMAN: All right. All right. If you want to jump ahead. Here is the steps of example 25. And

we've labeled them, we could go through all the chemical synthesis, and several of the experts will do that for you.

THE COURT: What is this, 62?

MR. SITZMAN: This is 62 but it doesn't disclose --

THE COURT: We are okay with 62?

MR. SITZMAN: I was just checking with them.

THE COURT: Okay.

MR. SITZMAN: Example 25 of the '737 patent. And what we've done here is broken it down as it's set forth in the patents as four steps 1, 2, 3, 4.

THE COURT: I think I have a different 62.

MR. ALY: Your Honor, I have that as 59. I don't know if the number is any different.

THE COURT: I'm going to follow what's on the screen but I think have a different one.

MR. ALY: It's 59 on my sheet, just to inform Mr. Sitzman.

THE COURT: Not a problem.

MR. SITZMAN: Let's go with 59.

THE COURT: I have it. It's 59. I'm good. I have it.

MR. SITZMAN: Batch 0, the step order for batch 0 if you look back in the laboratory notebooks is not 1, 2, 3, 4, it's 1, 4, 2, 3. There is an inversion of two steps.

It was a synthesis. It wasn't intended to be an example 25 but it was an early synthesis that Dr. Buschmann did. And really the only difference between example 25 and that is the switch.

THE COURT: So you are saying in the original lab notebooks it was actually 1, 4, 2, 3?

MR. SITZMAN: Well, in the lab notebooks there's a bunch of different synthetics. And batch 0, the one that corresponds with batch 0, if you try to compare it with example 25, what you see is it's 1, 4, 2, 3.

THE COURT: Okay.

MR. SITZMAN: Now you'll also see what ultimately becomes example 25 as well. But, if the court is interested in knowing how batch 0 was made, this is important.

THE COURT: I am.

MR. SITZMAN: The other thing that the Court's going to hear from the experts is this particular switch, 1,4, 2, 3, is akin to having coffee with cream and sugar, one adding cream and then sugar and the other one adding sugar and then cream. And the experts will explain that to you.

That was form B. That's what Dr. Gruss originally saw in form A . The resynthesis by Miss Mueller are represented here in the next two lines. And she carries out example 25, 1, 2, 3, 4 and she gets exhibit -- she gets form B.

THE COURT: Form B.

MR. SITZMAN: Now, these two in orange, since we

are jumping ahead, the two in orange represent the experiments that were conducted by the defendants' experts. The defendants bear the burden in this case by clear and convincing evidence to show that form A necessarily and inevitably forms when you practice example 25. That's their burden by clear and convincing evidence.

The Court will not hear any evidence from the defendants that the defendants ever performed example 25 from start to finish. Three defendants hired outside experts and no one started from the first step. No one. Their burden is clear and convincing evidence.

When they did buy the API and do Step 4, they got a mixture of A and B. Actually a few samples actually had more B than A. That's just a preview of what's to come.

I think the Court I think where we were in the invention story is Miss Mueller's resynthesis. Let my just go back to that real quickly. This might help.

THE COURT: I know what you're saying. You are saying we don't know what they started with so of course they got something different.

MR. SITZMAN: Correct, correct, correct.

THE COURT: But again just to clarify again with respect to the four steps, you say they were a bunch of lab notebooks and so on regarding the steps involved.

Tell me again, just clarify one more time how we

had the steps in example 25 versus whatever was done originally by Miss Mueller, 1,4,2,3, excuse me, she did 1,2,3,4 in September 2002.

MR. SITZMAN: Correct. When Dr. Buschmann originally started sketching out in his book, his lab notebook and decided he wanted to see what this compound was and could he do it, he sketched it out and he sketched out a synthesis and he sketched it out. And it's only in sort of a hindsight comparison here we are just comparing it so that you have a foundation for understanding the steps that are laid out for batch 0.

So when he originally sketched it out, he sketched it out for what would be 1, 4, 2, 3. Within the next few syntheses thereafter, he then sketches out 1, 2, 3, 4. That ultimately is what becomes example 25 in the patent.

THE COURT: Okay. So he starts with a different set of steps in terms of a different order. Not a different set of steps, a different order. He originally comes down to 1,2,3,4 and that's ultimately what's in example 25.

MR. SITZMAN: Correct, correct.

THE COURT: And that's what Miss Mueller does in 2002. She does 1,2,3,4 and she gets B.

MR. SITZMAN: Correct.

THE COURT: I'm with you.

MR. SITZMAN: Correct, correct.

THE COURT: Just going back, and I know there's some territory on this particular example that I'm not going to go into now that I will maybe go into on the afternoon session, but maybe we could talk about the Step 4 from the University of Wisconsin and Organix because that looks like there's a question mark here on this page.

MR. SITZMAN: So, they get, they buy the API Tapentadol and they then perform the final bromination step, I believe it's bromination, Organix, and they perform the formal purification step, the separation step, the crystallization step. It's all part of that last step process. And then they throw it through an XRPD machine so that they can analyze what it is.

THE COURT: Okay.

MR. SITZMAN: It raises the question as to why none of the defendants would have gone back and started at Step 1.

All right. Continuing on with the invention story, 2002, Miss Mueller confirms that example 25 yields form B. And it's at that point that Grunenthal realizes that form B was the original form, the original polymorph that Dr. Buschmann manufactured and sketched out here in synthetic chemistry. And that through the process of Grunenthal and further development, they had come across the more stable novel form, form A.

In June, 2004, Grunenthal filed for patent protection --

THE COURT: And more stable in terms of temperature?

MR. SITZMAN: Yes. You're going to hear some testimony about a few different, more terms, the terms are metastable and thermodynamically stable. Metastable means that it's still stable, stable at room temperature, stable. But it's not as stable as a different form. The form A turns out to be the more thermodynamically stable form of Tapentadol.

Since we are on that subject, it's my point of emphasis before, form B, even though it's metastable, was stable for eight years between the point in time Dr. Buschmann originally synthesized it and when the XRPD pattern was taken. So just because it's metastable, doesn't mean that there's something wrong with it or that there's some problem with it. Metastable just simply means that there is another crystal form that is thermodynamically more stable.

Now interesting enough, you are going to hear from Dr. Joel Bernstein who will tell you you can spend years looking for more thermodynamically stable molecules and never find it in which case the metastable form, because that's the only form you have, is considered the thermodynamically more stable.

THE COURT: Is considered what? What was the end

of that?

MR. SITZMAN: The more thermodynamically stable. If you only, if you keep looking and all you've got is one, it's got to be the more thermodynamically stable until you find something that's more thermodynamically stable.

THE COURT: Okay.

MR. SITZMAN: This is the patent, the '364 patent that we've talked about before. And that's the patent protection on polymorph form A.

Now, Grunenthal proceeded forward with its testing of Tapentadol and was moving forward with those nociceptive analgesic testings that I talked to you about earlier more formally at this point in time. But, in view of this, the unique properties of Tapentadol, Grunenthal wanted to conduct additional in vivo tests and they wanted to further characterize what this molecule could do.

Unfortunately Grunenthal had limited capabilities in terms of its in vivo modeling and in vivo testing in its facilities.

In 1996, Grunenthal hired Dr. Thomas Christoph, and the Court will hear from Dr. Christoph on Monday. Dr. Christoph was hired to build out a neuropathic department within Grunenthal.

The Court will hear from Dr. Christoph about a host of experiments that he designed, that he made, that he

performed, that he had his staff do. He started originally with some mononeuropathic studies. He's going to explain that. The Bennett and Chung models and all of this will become much clearer when you hear from him.

And then he moved on to polyneuropathic models and modified polyneuropathic models. The results and evidence from all of these tests was overwhelming. Tapentadol had a clear and significant effect on the treatment of polyneuropathic pain. In fact, Tapentadol ultimately outperformed morphine, the gold standard as I was telling you, in the treatment of polyneuropathic pain itself.

Dr. Christoph was able to show this through all of his tests. But he was also able to show some surprising and unexpected results beyond. He showed, and he will explain that Tapentadol had a higher potency, a higher potency for treating polyneuropathic pain over mononeuropathic pain.

What does that mean? It more easily treats the more complex pain syndrome than the easier and more simple pain.

THE COURT: So if you took it and you had something internal, an internal stimuli that you needed this for but you were injured, you would be able to feel the spot where you were injured?

MR. SITZMAN: That's excellent. That's my second point. That's the other surprising result. Because morphine

does not do that, by the way. Morphine, one of the downsides of morphine is that if you give enough of it you can treat your polyneuropathic pain but it will eliminate your ability to sense.

THE COURT: To sense.

MR. SITZMAN: Right. And you have people who will put their hands on a stove and they won't feel it or they will do something else. It's important to have that nociceptive pain transmission and response in order to keep the body together.

That's the second aspect of Tapentadol. It keeps that nociceptive pain transmission at its normal state while treating polyneuropathic pain, just like you said.

THE COURT: Okay.

MR. SITZMAN: The first bullet point though is you're looking at the models in terms of trying to treat one bundle of nerves versus many bundles of nerves. It has a higher potency, a higher tendency to treat at a lower dose the more complex nerve damage than the more simple nerve damage.

The other thing that Dr. Christoph discovered were several different synergistic effects that Tapentadol had within the animal models. And it provides some further explanation, as he will explain, to how Tapentadol functions in this unexpected way.

All of these discoveries led to the filing of the

'130 patent in March 2007 covering the method of using Tapentadol for the treatment of polyneuropathic pain and polyneuropathic pain associated with diabetes.

Let's talk about the patents now. The first patent, as I said, claims a discreet class of compounds known as 1-phenyl 3 Dimethylaminopropane compounds. That's the class of linear compounds that Dr. Buschmann identified and synthesized.

The Court as I said is going to hear from Dr. Buschmann about how he discovered these classic compounds, the claim at issue in the '593 patent. There's four remaining claims. Claim 8 is to a method of treatment using the class of linear compounds that Dr. Buschmann described and characterized.

Claim 61 is Tapentadol which was just one of the compounds in this family, claim 117 which is a method of treatment using Tapentadol and finally claim 147 which is a pharmaceutically acceptable salt of Tapentadol.

THE COURT: And the difference between 8 and 117 is what?

MR. SITZMAN: Claim 8 is to a genus, the family of compounds . Claim 117 which is a dependent claim --

THE COURT: Is specifically Tapentadol.

MR. SITZMAN: Exactly. The second patent and second invention is the '364 patent. This is the polymorph

patent. The claims at issue here are claims 1, 2, 3 and 25.

Claim one is to the crystal form, the stable form, crystal form A. And this is where I was telling you crystal form A that's characterized by eight specific peaks that are unique to form A. Claim two is also to form A with five distinct peaks on the XRPD patterns. And claim three is to crystalline form A, the pattern itself, actually the overall XRPD pattern being essentially the same as the XRPD pattern that is attached as Figure 1 to the patent. And 25 is a pharmaceutical composition comprising form A.

The third patent and the third invention is the '130 patent that I just spoke of. And the claims at issue are 1 and 2 which is the treatment of polyneuropathic pain using Tapentadol. And claims 3 and 6, which is the treatment of diabetic polyneuropathic pain using Tapentadol. I think I can do one more segment before we have to make a change.

THE COURT: Okay.

MR. SITZMAN: Very briefly, Depomed, in May 2015, Depomed purchased the Nucynta franchise from Janssen pharmaceuticals. The Court will recall Janssen was one of the original plaintiffs in the case, one of the plaintiffs. Grunenthal has and has been and still today a plaintiff.

In May 2015 Depomed purchased the Nucynta franchise for just over a billion dollars. And the Court will hear, probably after lunch, from Jack Anders the

vice-president of finance about that purchase and certain circumstances around that purchase.

Today Depomed and Grunenthal make and market Nucynta around the world, Depomed focusing here in the U.S. The generics, as the Court knows, would like to do the same. And with that I want to move on to infringement but I think we have an issue.

THE COURT: All right. Why don't we do this, we are going to take a break at this point and we are going to make arrangements. So we are going to go off the record at this point.

(Whereupon a short recess was taken.).

(Whereupon the hearing was under seal)

(Whereupon the following takes place in open court)

THE COURT: Anything else? No? We're all good. If we want to unseal it this portion, everyone is nodding yes. Anyone who opposes that. No one. All right. Let us unseal the courtroom.

The transcript is unsealed at this point as well it will be reflected on the record. So if there's anyone else that needed to come in, we can unseal the courtroom formally.

Let's continue.

MR. SITZMAN: Thank you, your Honor.

THE COURT: Thank you.

MR. SITZMAN: We now shift over to validity where the defendant's burdens are clear and convincing evidence. Defendants have challenged the validity of all three patents. Now, despite this burden, the primary art that the defendants are going to rely on, the primary pieces of so called prior art that they are going to rely on during the course of this case, is all art that was already before the examiner during the prosecution of all three of these patents.

The primary art that the Court's going to hear about from defendants is not new. In fact, as the court knows from the pretrial motions, the art that they are relying on for the invalidation of the '130 patent happens to be our own publications which also were before the examiner.

THE COURT: I do recall.

MR. SITZMAN: All right. Let's move on to the '593 patent. First, and primarily I think is their argument on obviousness. To establish obviousness of the '593 patent, the defendants must establish by clear and convincing evidence that there was a known compound in the prior art that would be the natural choice for further development. By the way, that's a known compound and motivation to modify that compound with reasonable expectation of success. That's called the lead compound analysis.

The Federal Circuit has coined that term and that's what they will use in terms of the law that applies to

this case. It is not the lead compounds analysis but the lead compound analysis.

Facing a virtual sea of endless possibilities, the defendants claim here that it would have been obvious to make Tapentadol. In 1994 there were thousands, thousands of starting places that a person of ordinary skill in the art looking to make a new analgesic compound could possibly start from, thousands.

By way of the thousands, defendants don't choose any one. Again it's a lead compound analysis. They must show you by clear and convincing evidence that there is a lead compound.

So, what do they talk about the most in their briefs and otherwise? They talk about Tramadol. Tramadol remember is a mixture of compounds. It's got the plus or 1R 2R and 1S,2S enantiomers and the metabolites. When asked which one of those is your lead compound, the experts all say um, all of them. They have to do that because you need all of them to get all of that activity.

Taking one of these molecules, though, and looking at it and trying to get from anyone of those four corners to Tapentadol without using any hindsight analysis is impossible. It was not obvious to make the necessary choices that one would have to make to get to Tapentadol.

The most important, which you've heard already

about this morning is it would not have been obvious to open that cyclohexane ring. The contrarian arbitrary choices that you would have to make in order to go from anyone of these let alone all of them to Tapentadol goes against the scientific principles and there's absolutely no motivation or even suggestion that you would do that.

The Court, as I mentioned, will hear from Dr. Bill Roush, Professor of chemistry and director of medicinal chemistry at Scripps. And he will testify that none of the choices were obvious, let alone all of the choices that would have to have been made to get to Tapentadol. No one would have made those choices for good reason.

Enablement. Defendants assert that the genus, that's the claim 8 that has the family of compounds, they argue that that claim 8 is not enabled. The patent discloses multiple synthetic methods of making the various compounds that are in the genus of claim 8, one of which as you know is example 25 to make Tapentadol. But there are other synthetic rounds and other syntheses that are disclosed in the patent.

Defendants admit that making the compounds that would fall into claim 8 would be routine. It would be routine for a synthetic chemist to make those. What do they argue? The defendants argue it would be routine to make a compound that falls within. It would be undue to make all of those compounds. And you are going to hear testimony from the

defendants' expert talking about oh, there's tons of compounds that are claimed and that are part of this genus. And it would take undue amounts of time to make them all and test them all.

That's not the law. The law is that you don't have to make all the compounds of the genus and test all the compounds. It has to be something that routine experimentation by a person of ordinary skill in the art can do and test for themselves compounds within that genus.

Written description. You will hear the defendants experts testify that a person of ordinary skill reading the patent would not have had any belief that the patentees actually possessed the invention.

Defendants continue to argue, notwithstanding the claim construction order, that the wrong name for Tapentadol and the melting point, that is erroneously recorded in the patent, somehow destroys this patent and it establishes a lack of written description.

Defendants are grasping at straws here. There's little doubt that the patentees possessed this invention there's. Little doubt that the patentees knew what they had made and ultimately commercialized one of those products.

Utility --

THE COURT: You know what, can we go back to Tramadol for a second? We discussed how it's a mixture of the compounds and that it metabolizes in a certain way.

Why would defendants not be permitted to look at that in terms of a lead compound? I know you had used the word very specifically "compound" as opposed to "compounds". But is there any history in terms of you know the caselaw on this that discusses this particular issue, meaning a substance versus a compound?

MR. SITZMAN: I'm not aware of any. The Federal Circuit has said that you need to identify some -- because that's how the analysis has to start, some individual lead compound so that one can analyze the modifications that would be necessary in order to get to the compound.

THE COURT: Right. And I understand the lead compound analysis. But the distinction between a compound and this particular, I'm going to call it a mixture.

MR. SITZMAN: Exactly.

THE COURT: If you would focus in a little bit about again how you see the distinction there. And based upon whatever exists in terms of legal authority, how you would see that. I know you are doing your opening but I'm just curious if there's anything that you would like to discuss with respect to that.

MR. SITZMAN: I think the best way to do it is to suggest how you might approach it but why that would be wrong.

Each one requires some modification to get to Tapentadol. There has to be choices that need to be made

along the way and they have to be motivated and lead to some reasonable success.

But in order to take this mixture and get to Tapentadol, then you'd have to modify all four, you would have to explain why or how all four would either independently get to Tapentadol or how collectively they would get to Tapentadol. And then what you've done is you've again now made this lead compound into a multi-tiered analysis of multiple molecules all leading someplace and with an explanation that would have to support each one.

THE COURT: When you ingest this what are you ingesting? The left and the right on the top?

MR. SITZMAN: The enantiomers.

THE COURT: Okay.

MR. SITZMAN: You are ingesting those. You know, you are making the metabolites and you want, presumably, the analgesic activity and need all four.

Utility. Defendants claim here that the invention is not useful to the public. The patent discloses in vivo animal data for 24 of the claimed compounds. That is not enough, defendants say. They contend that the patentee here needed to demonstrate pronounced analgesic activity which was discussed in the summary section of the patent.

But this is nowhere to be found in any of the claims. This is just defendants grafting in new limitations

to patent claims and asking the patentee to demonstrate something that's not there. This is a useful compound to the public.

All right. Let's move on to the '364, unless you have questions.

THE COURT: No, I'm good. Thank you.

MR. SITZMAN: Okay. The '364 patent, there are three points of attack here, inherent anticipation, obviousness and unclean hands. Let's take them in order. In inherent anticipation that the prior art necessarily, I think I alluded to this earlier, necessarily and inevitably produces polymorph form A. This is the seminal case Schering Plough.

To succeed, the defendants have to show by clear and convincing evidence that the prior art necessarily and inevitably produces form A. They were relying on example 25. And not any one of the defendants and not any one of the defendants' experts ever went back to the beginning.

The evidence that we've demonstrated, even though it's not our burden, is that example 25 yields form B and we have evidence and we will put on that evidence that they will not be able to overcome.

You know what, I didn't get a chance to talk about this in case the Court was asking me --

THE COURT: The pressure study.

MR. SITZMAN: Yes.

THE COURT: Go ahead.

MR. SITZMAN: Well, you heard a little bit about it.

THE COURT: I did.

MR. SITZMAN: But admittedly that is not a full and faithful performance of all five steps. However, Miss Mueller, when she did do that experiment, did what the defendants did, and she got form B.

All right. Let's turn to obviousness.

THE COURT: So, wait a minute, in terms of what Miss Mueller did --

MR. SITZMAN: In 2009.

THE COURT: We have question marks for her steps. What are those steps? Are you are saying they are the same steps the defendants engaged in?

MR. SITZMAN: We don't know for sure but it's roughly the same approach, which is to get the API from someplace else. Someplace else that we don't know how the API was made and then do the last step. And then everybody is going to say the API I got was the right thing. It was Tapentadol. But nobody can tell you that the API they got performed steps 1, 2 and 3. And there's no evidence or suggestion that it did follow. In fact, there's evidence that it didn't follow 1, 2 and 3.

THE COURT: And she only received a result of B

on that?

MR. SITZMAN: Correct, with no A.

THE COURT: I'm good. Go ahead.

MR. SITZMAN: All right. We're moving on to obviousness. In one of the most unpredictable fields in the pharmaceutical industry the defendants claim that it would have been obvious to make form A. That's the obviousness claim.

The Court will hear testimony from one of the foremost authorities in polymorphism, Dr. Joel Bernstein. He will be here in a week or so to testify about how a person of ordinary skill would have had no way of reasonably knowing or predicting that form A of Tapentadol existed or how to get it.

Let's look at this step wise. This will show you, starting with the family of compounds that are disclosed in the '737 patent, the first step in this obviousness analysis would be to find and pluck out Tapentadol out of this family. There's nothing that suggests in the '737 patent, that somebody should take Tapentadol out. So, that's the first step.

Then there's no way to predict at that point in time what will result in terms of solid state analysis whether there's going to be hydrates, solvates, polymorphs or none at all.

So, we are just going from this step, assuming somebody had actually picked out Tapentadol, they would have to

try to predict reasonable predictions, at least as to what would come out in solid state. Assuming then that they reasonably were able to predict polymorphs, then the question is how many. How many polymorphs are there going to be 1, 2, 3, 4, 5, 6.

Dr. Bernstein is going to tell you about situations where we have 13 polymorphs. He is going to tell you a case that off with Retonavir where they started down the road where the polymorph changed over to another and another and another and could never get back to the original polymorph. This is a very unpredictable field.

But, let's say, let's just say the person was able to pluck out Tapentadol, was able to predict that polymorphs would result and was able to predict that two polymorphs would result, then you have to then go to a structures of properties analysis that this person, this person of ordinary skill in the art would also have to predict. Because it's only from that stage that you would get to the analysis of what's the most stable form. And then, assuming you've made all of these predictions perfectly, you will get to form A.

This is defendants' claim that form A was obvious in light of the '737 patent.

Now, instead of dealing with all of this and explaining how you could possibly get through this tree, the defendants' position is very simple, it would have been obvious

to do, all the tests would have been necessary, and you would simply test and test and test and test and then at some point in time you would get form A.

Obvious to do a test is not the law. It's never been the law. Not under KSR. Not in the past. Not in the present. There is no way to reasonably predict form A of Tapentadol from starting with the '737 patent.

Now the third ground --

THE COURT: I'm sorry, the Buschmann family that we are talking about, how many compounds were contained therein?

MR. SITZMAN: Well, if you listen to defendant's experts, I think Dr. Wolf, he will testify that there is hundreds of thousands, millions that would fall within that genus of compounds. Actually that's just claim 8.

Within the entirety of the patent, there's probably millions of potential linear compounds.

THE COURT: I'm sorry, millions in the entirety of the patent?

MR. SITZMAN: Yes. Dr. Wolf I think tried to analyze that by just looking at claim 8 as opposed to looking at the entirety of the patent. But, under this analysis when you are looking at trial to figure out how you go from the '737 patent to a polymorph, you don't have that luxury of knowing that claim 8 will at least reduce some of that. Unless of

course I guess someone could predict that claim 8 was relevant out of the 140 something claims. Sorry, that's wrong. At the time of the '737 patent there was only 8 claims.

THE COURT: Okay. And the defendants' testimony of Dr. Wolf is regarding claim 8?

MR. SITZMAN: Yeah, I think so. I don't think he is offering an opinion as to the entire patent. But, I don't think it will make much of a difference. I think you will hear there are millions of compounds.

THE COURT: Okay.

MR. SITZMAN: The last argument that they are making here for invalidity is the one that Roxane is advancing and that is unclean hands. This is an enforceability argument claiming that the '364 patent is unenforceable.

The Court's already heard and seen a preview of this argument so I'm not going to go through it. The evidence through the course of the trial though will show that plaintiffs did not engage in the egregious misconduct that is required for unclean hands. And there will be no evidence, during the course of this trial, that Grunenthal, of Grunenthal's intent to mislead the Patent Office. There will be a complete failure on intent.

All right. Let's move on to the '130 patent. Defendants claim that the '130 patent is both anticipated and obvious. Again the art that they are relying on is not

independent art that was not already considered by the examiner. No. In this instance they are actually relying on Grunenthal's own work, the Tzchentke references, to invalidate the patent.

Now as the court knows from our pretrial motion papers on these references to Tzchentke down here you can see at the bottom right, those are not prior art. They constitute the work of the Grunenthal inventors? And that work, sorry -- can you go back one more.

That work was done well after the invention was conceived and the invention was reduced to practice. So whether you analyze this on a concept reduction to practice or because these pieces of prior art that they are relying on are that of the inventors, either way these references are not prior art for purposes of anticipation and obviousness.

What's defendants' argument? The defendants' argument is well, the Tzchentke references are authored by people and there are authors that are not inventors. That fact alone, by the way, doesn't convert the Tzchentke references into prior art because, for among other reasons, defendants have not and cannot identify anything in the Tzchentke references that comes from a non inventor that is part of or related to the '130 patent.

Let me say that again. '130 that last and that piece of analysis is important. They cannot identify something

in the Tzchentke references that come from a non inventor that is either in the '130 patent or that relates materially to something in the '130 patent.

THE COURT: So everything in the Tzchentke references are to Tzchentke himself on the '130 patent or they are not material. Is that it?

MR. SITZMAN: Of sort. There is some other disclosure and either they are not in the '130 patent or they are not relevant to the '130 patent. There are other authors on the papers other than Tzchentke. We keep using Tzchentke as a shorthand because he is the first author. And Dr. Tzchentke who you will have testimony from by deposition, is a Grunenthal employee.

That last step of the analysis that I said was so important is because otherwise if you can't tie something from the Tzchentke references, if that's what you are relying on, to something in the '130 patent from a non inventor that happens to be a co-author, if you can't do that, you can't use it in any way to try and invalidate.

And we asked defendants' experts did you do that last step of the analysis. Can you identify something in the Tzchentke references from a non inventor that has shown up or appeared in or related to the '130 patent. And Dr. Buvanendran said I didn't do that analysis.

Last one. Obvious double patenting. Defendants

will claim that a person of ordinary skill would have understood the '737 patent, that original Buschmann patent, to cover the use of Tapentadol for the treatment of polyneuropathic pain. There's nothing in the '737 patent that remotely points to or suggests that Tapentadol can be used to treat polyneuropathic pain.

There is data, I think I told you there is data in one '737 patent. It's the mouse writhing data. It's the nociceptive model that was used to see in these linear compounds that had analgesic activity.

That doesn't tell you anything about whether neuropathic pain or polyneuropathic pain can be treated using any of these compounds. In fact, if that were the case then Dr. Christoph wouldn't have had to spend 12 years doing all kinds of tests to try and characterize this and see whether or not did it treat polyneuropathic pain.

There's nothing obvious about the Tapentadol ability to treat polyneuropathic pain. And there was nothing predictable about the results and the unexpected results that Dr. Christoph found.

Again, I think the Court will recall the unexpected results that were discovered, the higher potency for polyneuropathic pain to treat polyneuropathic pain over mononeuropathic. The ability to treat polyneuropathic pain and keep the nociceptive pain transmission at its normal state

and the synergistic effects within the compound.

Now, your Honor, at the end of the trial, we're going to be asking your Honor to find that defendants' ANDAs infringed all three patents and that all three patents are valid and enforceable. And in view of all the evidence that's going to be presented, we're going to ask the Court to order that the effective date for the approval of any and all of the defendants ANDAs be no earlier than the date of the original patent expiration as extended through various extensions that have been granted by the PTO and FDA.

And if the Court doesn't have any further questions, I am through.

THE COURT: I'm fine. No further questions on this end. I do appreciate your presentation. Thank you very much.

MR. SITZMAN: Thank you.

THE COURT: I listened very carefully. So that concludes on behalf of, is it just with respect to Depomed or is it with respect to the entirety of the plaintiffs at this point?

MR. LEWRIS: Entirety of the plaintiffs.

THE COURT: Much appreciated. I think we should take our break at this time and then we can hear from the defendants. I think you probably have three presentations about a half hour apiece. Is that right? Everyone is nodding

yes. And I look forward to those as well. Thank you in advance.

Why don't we do that, we will take a break for about 45 minutes. I think the lunch has already arrived. Whoever has ordered lunch, I think it's already here. You know which rooms you are going to. So that should work out just fine. And we will see you back here in 45 minutes. 1:30 sounds good.

(Lunch recess)

THE COURT: My deputy just informed me that it sounds like we might have to engage in a clearing of the courtroom. Is that correct?

MR.FITZPATRICK: About a third of the way into my opening.

THE COURT: Oh, all right. So you'll let me know then.

MR.FITZPATRICK: I will, your Honor.

THE COURT: Very well. Okay. And before we turn to defendants, I just have one quick question for the plaintiffs and it's right at the end of the slides. It's page, it's on my slide book it's a little bit off, I think, from the ones that were on the screen 66, the critical data. Did you define --

MR. SITZMAN: It's the latest data that we reduced to practice the polyneuropathic pain model and demonstrated

that it worked. You will hear all of about this, but the STZ model rat --

THE COURT: STZ model.

MR. SITZMAN: Rat. You will hear from Dr. Christoph that is a model of polyneuropathic pain. And that we completed it no later than that and demonstrated that it worked in the polyneuropathic model.

THE COURT: So that's the latest date then that you're referencing?

MR. SITZMAN: Exactly. Exactly.

THE COURT: All right. Thanks for that.

MR. SITZMAN: Thank you.

THE COURT: Let us begin. Let's turn to the defendants. How are you going to divide the argument?

MR.FITZPATRICK: Your Honor, Anthony Fitzpatrick for Actavis.

THE COURT: Yes. Thank you.

MR.FITZPATRICK: I'm going to proceed first.

THE COURT: Okay.

MR.FITZPATRICK: Then Mr. Schuler for Roxane and then Mr. Aly for Alkem.

THE COURT: Very well. Thank you. You may proceed.

MR.FITZPATRICK: Thank you, your Honor.

THE COURT: Thank you.

MR.FITZPATRICK: Your Honor, I have copies of my slides.

THE COURT: Thanks so much. You can send them up.

MR.FITZPATRICK: May I proceed, your Honor?

THE COURT: Yes. Thank you.

MR.FITZPATRICK: Thank you, your Honor.

MR. SITZMAN: Sorry, your Honor, if we can, we are just getting the demonstratives. If we can just flip through.

THE COURT: Absolutely. Take a moment. Let me know if there's any issue with respect to them.

MR.FITZPATRICK: Your Honor, the confidential portion will begin, I think, at slide 19.

THE COURT: So, just as we approach that, I ask you to be mindful of it and you let us know and we will engage in the same process as we did this morning.

MR.FITZPATRICK: Certainly.

THE COURT: Thank you.

How are you doing with that?

MR. SITZMAN: It doesn't look like anything is problematic.

THE COURT: Excellent. Let's begin.

MR.FITZPATRICK: As I said, Anthony Fitzpatrick from Duane Morris on behalf of Actavis Elizabeth.

I want to briefly introduce our team. You know Mr. Capuano and Miss Wiggins who are our local counsel. And Carolyn Alenci from our team is here in the back of the courtroom. And we do have one other person on our team who is not here today but who will be here next week Patrick Gallagher.

THE COURT: Thank you.

MR.FITZPATRICK: We represent Actavis Elizabeth LLC. Actavis is a global leader in genetic pharmaceuticals. And its U.S. headquarters are located near here in Parsippany, New Jersey.

This case relates to, as your Honor knows, Tapentadol hydrochloride. And in particular there are three approved products with that active pharmaceutical ingredients. There are immediate release Tapentadol hydrochloride tablets which are marketed by the plaintiff Depomed under the trade name Nucynta. There's an oral solution of Tapentadol. And then there are extended release Tapentadol hydrochloride tablets which are sold by Depomed under the trade name Nucynta ER.

And there are, as your Honor has heard many times, three patents-in-suit. What we all refer to as the '593 patent which is a reissue patent which claims Tapentadol hydrochloride itself. The '364 patent which claims a specific crystal form of Tapentadol hydrochloride which we all refer to

as form A. And then the '130 patent which claims methods of using Tapentadol hydrochloride to treat polyneuropathic pain. These patents are owned by the plaintiff Grunenthal and licensed to the plaintiff Depomed.

This slide shows the expiration dates for the three patents and also what their respective listings are in the FDA's orange book. The '593 patent will expire in 2022. It has been listed in the FDA orange book for immediate release tablets, extended release tablets. And the oral solution.

That's also true for the '364 patent which will expire in 2025. And then the '130 patent which will expire in 2028 is only listed in the orange book for extended release tablets.

So, how did we get here? How did we get to this point where we have three patents asserted against these defendants? Well, the history starts as Mr. Sitzman indicated this morning, back in the 1960s when Grunenthal developed Tramadol. And in 1972, Tramadol was patented in the United States, the United States patent Number 3652589 claiming the compound Tapentadol. And that patent expired in 1989.

And this is that original patent the 1972 patent for Tapentadol, I'm sorry, for Tramadol which issued from an application that had been filed in 1964. In 1977 Tramadol was approved in Germany. And in 1978, the inventors of Tramadol published prior art . And this is prior art that I'm going to

come back to later in my presentation, but it's important prior art because they disclosed a great deal of information regarding the structure activity relationship for Tramadol.

So, chemists talk about structure activity relationships and that means if you've got a certain structure of a chemical molecule, what's the activity of that molecule. What does it do? And if you change the structure in some way or ways, what does that do to its activity? And these inventors published the paper that I will come back to later, the Flick paper in which they talked about that.

And as the '589 patent, the patent that had issued in 1972 neared its expiration, Grunenthal undertook what it itself called the Tramadol successor project. And they initiated this project because they had good sales success as they said themselves in the introduction, in the very first sentence. Only the good sales success of Tramadol in the last few years has underlined the desire for a Tramadol successor.

They also had a good understanding, as I say, of the structure activity relationship of Tramadol because their inventors had studied that. And they pointed that out right here. They said the chemistry has synthesized a variety of compounds based on the Tramadol molecule.

And they were also concerned about not having a patent protected product. And so they decided to start with the activity profile of Tramadol as a starting point for the

successor. And Tramadol was known, at that time, to have a special place among analgesics because it has this dual method, this dual mode of action having both opioid activity and non opioid activity.

And in their successor project Grunenthal developed a desired profile for this successor product and they in fact formulated what they themselves refer to as the ten commandments for this project. And they laid out the particular profile and the particular criteria that we're looking for. And Number 9 was, the substance should be patentable. They wanted something that would be patentable.

And in order to obtain such a substance they set out to systematically vary, in their words, systematically vary the control structure of Tramadol. And the outcome of that project was Tapentadol. The '737 patent application was filed for Tapentadol in 1995 and then that issued in 2001. Subsequently in 2003 they sought a reissue of that '737 patent and that reissue is the '593 patent which is one of the patents here in suit.

Then four years after that, in 2011, they obtained the '364 patent and then again in 2013 they obtained the '130 patent.

Now, one point that's important here to notice that the '737 patent is prior art to both the '364 patent and the '130 patent because of the timeline and because of when

those later applications for those later patents were filed. The '737 patent which was later reissued as the '593 is prior art to the '364 and the '130.

THE COURT: Okay. And the reason for the reissuance?

MR. FITZPATRICK: I think some of my colleagues are going to get into what happened in the course of the reissuance later on.

THE COURT: Okay.

MR.FITZPATRICK: But, one thing that this shows is the lengths to which Grunenthal has gone and would go over the course now of more than five decades to maintain patent rights for its analgesic portfolio. So let's talk about these three patents. Let's begin with the '130 patent.

The '130 patent has only method claims. It claims methods of treating polyneuropathic pain comprising administering Tapentadol. I have up here on this slide 14 claims 1, 2 and 4 of this patent. Claims 1, 2 and 4 have been asserted against Actavis.

Mr. Sitzman didn't talk about claim four so I will focus on 1 and 2. But, I think the analysis will be the same regardless. These are first and foremost method claims. There's no allegation that Actavis would or could directly infringe these claims because Actavis is never going to administer this drug to a patient. Actavis makes and sells

the drug.

And so the claim against Actavis and against the other defendants is a claim of indirect infringement which is either inducement of infringement under 35 USC section, 271(b) or contributory infringement under section 271(c).

So let's talk a little bit about those statutes and the law relating to inducement and contributory infringement.

First of all the federal circuit tells us that in order to prevail on an inducement claim the patentee must first establish that there has been direct infringement. So they have to show direct infringement first. And then secondly they have to show that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement.

And we have some guidance from the Federal Circuit on what that means in the Hatch-Waxman context. And this is the Takeda pharmaceuticals versus West-Ward case from just last year. Because in Hatch-Waxman cases where there are method of use claims, the whole issue of does the label induce is frequently an issue.

And in the Takeda case, the Federal Circuit says the label must encourage, recommend or promote infringement. And they held that merely describing an infringing mode is not the same as recommending, encouraging or promoting an

infringing use or suggesting that it should be performed.

And the federal circuit went on in Takeda to say, as we have stated in Warner Lambert in the ANDA context, it is well established that mere knowledge of possible inducement by others, infringement by others does not amount to inducement, specific intent. And action to induce infringement must be proven.

And then from the Warner Lambert case itself the Court tells us that where a product has substantial non infringing uses, intent to induce infringement cannot be inferred even when the defendant has actual knowledge that some users may be infringing.

So, a lot of focus and a lot of emphasis from the Federal Circuit on the intent requirement and teaching from the Federal Circuit in the context of inducement that if you have substantial non infringing uses, you can't infer intent.

Moving now to contributory infringement under 35 U.S.C section, 271C, I've got the statute itself on this slide. This statute, this section to me is always kind of a mouthful. But, there are really, I think, two important requirements that have to be established by the patentee in order to prove contributory infringement.

First of all, they have to show that the alleged infringer knew that the accused product was especially made or especially adapted for use in an infringement of such patent.

So there's a knowledge requirement that it is especially made and especially adapted to be used in infringement. Secondly, they have to show that it's not a staple, article or commodity of commercial suitable for non infringing use. So, if it is suitable for non infringing use or substantial non infringing use, then there cannot be contributory infringement.

And the Supreme Court has told us that 271 C requires a showing that the alleged contributory infringer knew that the combination for which his component was especially designed was both patented and infringing. You have to know that not just that there's a patent out there, but the product, if used, would infringe.

So, now, your Honor, I am approaching the point of confidential material.

THE COURT: Very well. Let us pause for a moment on the record. We will go off the record. Actually we will stay on for one moment. Does everyone agree at this portion we should seal the courtroom? If you'd like to take a look at the slide that we are up to. We are up to 18 . So you can take a look and let me know.

MR. SITZMAN: We don't have any objection if Actavis wants to do that.

THE COURT: All right.

MR. SCHULER: Same for Roxane.

MR. ALY: Same here.

THE COURT: Very well. We are going to seal the courtroom at this point. So, what I would ask that our counsel take a look to see whose remaining in the courtroom, identify their representatives who may remain and everyone else will remain outside until the record becomes open again.

How should we handle it? Do you want to do the same thing I did before? Let's see, who's from Depomed, stand up please. We will just do this really fast. From Grunenthal, stand up. Who do we have from Actavis? Please stand. Okay. Roxane, please stand. And Alkem, please stand. All right.

Everyone is standing. No one is seated. You recognize everyone in the room. Everyone knows who their people are. All right. Very well. The courtroom is sealed. Thank you.

MR.FITZPATRICK: Thank you, your Honor.

THE COURT: Thank you.

(Whereupon the hearing is under seal)

(Whereupon the following takes place in open court).

THE COURT: I think you can go ahead.

MR.FITZPATRICK: Thank you. I will move now to the '593 patent. We will call to testify regarding the '593 patent Professor Stephen Martin. Professor Martin is a

professor in the department of Chemistry at the University of Texas at Austin. And he will testify and explain to the court that in his view the '593 patent claims are structurally obvious in view of the lead compound Tramadol.

So let's go back and talk more about Tramadol. Tramadol was clinically proven to be safe and effective as an opioid based analgesic to treat moderate to severe pain. I will also just note that to address a question that you had of Mr. Sitzman this morning, that my recollection is that Tramadol has also been used to treat polyneuropathic pain.

As I explained earlier, Tramadol was patented in 1972, approved for use in Germany in 1977. And in 1978, as I will explain further in a moment, the structure activity relationships of Tramadol were extensively studied and that work was published. And as I say the structure activity relationship is what's the relationship between the structure and any changes you make to the structure and the activity and any changes in the activity.

And among the Mr. Sitzman's huge field of analgesics, Tramadol was really unique. Tramadol was at the time the first and only analgesic to combine these opioid and non opioid mechanisms of action.

And accordingly, a person of ordinary skill in the art knowing that and knowing the prior art that had been published about it, would be motivated to, would want to

maintain what was unique about Tramadol but search for new and improved analgesics.

Now, Tramadol was known to have these two enantiomers. The RR Tramadol enantiomers and the SS Tramadol enantiomer. And then when administered to a human, those two enantiomers would metabolize to RR O desmethyl Tramadol and SS O desmethyl Tramadol. And that just means in the liver this OCH-3 up at the top gets knocked off and replaced with a hydrogen.

These molecules, these four molecules were studied extensively in the prior art individually and collectively. They were studied so that it could be understood how they work, which components of the molecules contribute to their analgesic effect, and which components contribute to which effect the opioid and the non opioid.

And the prior art describes the interactions between the enantiomers of Tramadol including potency activity and side effects.

So again a person of ordinary skill in the art would be interested in developing Tramadol analogs that would maintain its analgesic potency but reduce the side effects.

THE COURT: In the course of your discussion if you could distinguish and present your position with respect to compound versus compounds in terms of examining prior art. We touched upon that earlier this morning.

MR.FITZPATRICK: I was just going to approach that, your Honor.

THE COURT: Very well. Thank you.

MR.FITZPATRICK: Because the law is what would a person of ordinary skill in the art do. And Professor Martin will explain that a person of ordinary skill in the art, knowing what was known, would look at the mixture, all four together, and would look at the individuals and he will testify about that. And specifically --

THE COURT: And in terms of any caselaw that you'd like to cite to in materials of what is the best way for the Court to approach the issue of a lead compound, whether it's singular, whether it's plural, whether it's one molecule, whether it's more than that, do you have anything that you'd like to point to as being particularly apt in this circumstance?

MR.FITZPATRICK: Nothing comes immediately to mind, your Honor, but, we can certainly take a look at that.

MR. SCHULER: I can briefly address that.

THE COURT: Yes. Go ahead.

MR. SCHULER: From Roxane's perspective it would be M.S. versus Teva case. We will happily give you the cite to that, cited by the Federal Circuit last year. And hate to do it from memory because if I'm wrong, I will be called out about it.

THE COURT: That's okay. We can clarify tomorrow. But, go ahead.

MR. SCHULER: Two of the attributes the Federal Circuit looked for were A, structural similarity between the potential lead compound and the subject matter of the claim and whether there would have been a reason to modify the prior art compound such that it would be a promising lead compound.

And I think there's some generalized language about a lead compound versus the lead compound. And I believe counsel for the plaintiffs suggested that the answer is the lead compound. But I believe the Federal Circuit at least on one occasion in that case used the phrase a lead compound.

THE COURT: Okay.

MR. SCHULER: I will let Mr. Fitzpatrick address the indications of that.

THE COURT: Okay. Thank you.

MR.FITZPATRICK: So, in particular, of those four, so just going back to the four for a moment, of those four, a person of ordinary skill in the art would have known a lot about and focused on the RR Tramadol and the SS O desmethyl Tramadol because those were known to have these combined two effects, the opioid and the non opioid mechanisms of action.

And in particular --

THE COURT: So you're saying that someone would focus on the metabolite as well?

MR. FITZPATRICK: Yes, your Honor.

THE COURT: That would be the primary choice to start with, those two?

MR.FITZPATRICK: It's certainly, yes.

THE COURT: Okay.

MR.FITZPATRICK: And so the metabolite would be of particular interest because it would avoid some complications that were known. And it would also, it was known that the metabolite had a three fold, it was three times more active than its parent.

So, again this was known since the 1970s and it was known from the prior art that there were certain components of the molecule that were what Professor Martin will describe as the Tramadol pharmacophore. These are the components of the molecule that are essential to its properties.

A person of ordinary skill in the art would know that he or she could do something, could modify the molecule by doing something with this hydroxy group right here or this ring down here. And so this shows the movement from the SS O desmethyl Tramadol to what is in Tapentadol.

And again the highlighting here shows the changes that a person of ordinary skill in the art would make from Tramadol to Tapentadol and note that throughout the pharmacophore the essential components of the molecule remain intact.

Now, Mr. Sitzman talked about a move to a linear structure. Professor Martin will explain that a linear structure is a common theme in compounds that act on the neuro epinephrine receptor. So that was something that was known. And if you were trying to design a compound to act on the opioid receptor and the neuro epinephrine receptor, you would want flexibility in the linear compound.

But again notwithstanding this talk about linear, what's important is that the pharmacophore remains intact. The core, the key parts of the molecule remain intact.

THE COURT: When you say the linear structures, the common theme, if you could be more specific on that.

MR.FITZPATRICK: Just that that was something that was known in the field in the prior art. It was known that if you wanted to act on the neuro epinephrine receptor, having a linear structure would be desirable. That was something that was known in the art.

So the critical prior art here comes from the inventors of Tramadol themselves. This paper from 1978, by Flick, Frankus and Friderichs reports on structure activity study for Tramadol and related compounds. This is the single most important piece of prior art as to the '593 patent from the inventors of Tramadol. And it defines, again, the pharmacophore of Tramadol.

It defines the components of the molecule that is

essential to its activity. This is not prior art that relates just to the thousands of analgesics generally. This is prior art that relates to these types of compounds specifically. It shows the importance of specific components of the compound and it is the most relevant structure activity study for that class of compounds.

Professor Martin will also talk about another paper from 1978, the Frankus paper again from an inventor of the '593 patent. And Professor Martin will testify that this prior art describes the importance of the relative stereochemistry of Tramadol. So a person of ordinary skill in the art would know that they couldn't change the relative stereochemistry of the enantiomers. You would still want an RR and an SS. You wouldn't want an RS and an SR or something like that.

So, this slide, there's a lot going on here. But, this really is a summary of the changes that a person of ordinary skill in the art could make to improve the analgesic properties of Tramadol. A person of ordinary skill in the art, as we see in red, would not change the amine nitrogen region, which is the phenyl region which is up here, or the stereochemistry region. But, they could change the bridge carbon region or the cyclohexane region.

And a person of ordinary skill in the art would be motivated to make these changes and would have a reasonable

expectation of success, as Professor Martin will explain, and the result would be Tapentadol.

And so he will explain that the claims of the patent are obvious in view of that Tramadol prior art. None of this is hindsight. Professor Martin's analysis was not conducted with the benefit of any information relating to the Tramadol successor project.

THE COURT: I'm sorry, which witness is testifying about what you believe a POSA would or would not change?

MR.FITZPATRICK: Professor Martin.

THE COURT: It is Professor Martin.

MR.FITZPATRICK: Yes. So finally, your Honor, the '364 patent which is as we refer is directed to a crystalline form, form A of Tapentadol hydrochloride.

We will call to testify regarding the '364 patent Professor Mark Hollingsworth who is a professor of chemistry at Kansas state university. And he will testify that the '364 patent is anticipated and obvious in view of Grunenthal's '737 patent.

So, again, the '737 patent that we've talked about, you've heard about here, it was issued in 2001. So it's prior art as of 2001. And it claims Tapentadol and it includes in its examples various methods of making Tapentadol. And one of those is example 25 which is right here and you've

heard a lot about example 25. You will hear a lot about example 25.

THE COURT: I suppose.

MR.FITZPATRICK: One thing that's important to bear in mind in approaching and thinking about the '364 patent is that the claims cover any amount of form A. There's no requirement of any specific amount. There's no threshold. There's no concentration requirement. Nothing like that. It's any amount of form A.

The defendants will present evidence of two recreations of sample 25. And we'll show that those recreations produced some form A. Professor Hollingsworth will testify about recreation that was done by a company called Organix and Chemic and he analyzed the results of that and this is from his report. This is the result of an x-ray powder diffraction analysis of the sample prepared according to example 25.

And Professor Hollingsworth will explain that the peaks that are shown here demonstrate that the result included form A. We will also hear testimony from, and I leave it to my co-counsel on the defense side to talk about another recreation by the University of Wisconsin.

THE COURT: But, in terms of the starting substance that was used to recreate, was that a purchased substance?

MR.FITZPATRICK: I'm sorry.

THE COURT: The starting substance that was used to recreate.

MR.FITZPATRICK: The starting substance was a purchased substance. You know, I'm sure your Honor has already heard a lot and will hear more about steps 1, 2 and 3. It's, oh my gosh, they didn't faithfully do 1, 2 and 3. There are two important points to keep in mind here, your Honor. First of all, Step 4 is the critical step here. Step 4 is the step that involved demethylation and salt formation. And that that's the step that determines what the polymorph is. That's the critical step.

Saying that we didn't faithfully, properly implement example 25 because we didn't do 1, 2 and 3 is akin, I would submit, your Honor, to saying you didn't properly bake your cake because you didn't grow the wheat and you didn't mill the flour from that wheat.

It's those steps are not significant compared with Step 4. Step 4 is the significant step. And there is no allegation, no contention, no argument that Step 4, as performed by Organix did not faithfully follow what's set forth in example 25 .

And so we will demonstrate that the natural inherent inevitable consequence of following that process is the production of form A. And hence that example 25 inherently

anticipates the claims of the '364 patent.

It's also important, your Honor, to note and Mr. Sitzman spoke to this this morning, form A is the more thermodynamically stable form of Tapentadol. It's the form that is stable at room temperature. Form B in a chemically pure form only exists at temperatures well above.

THE COURT: Go back to the source substance again. In terms of that, do you do any examination on it once you get it before you do this further, you know, the further analysis through the rest of the steps up through Step 4, to determine what it is you've obtained and if it is in fact the desired substance?

MR. FITZPATRICK: Sure.

THE COURT: So how would you determine how that has form A in it or form B in it or something that might produce that ultimately at the conclusion of your process.

MR.FITZPATRICK: Well, I may ask for some help from Mr. Capuano on this one.

THE COURT: Okay.

MR. CAPUANO: Your Honor, thank you. The material that was purchased and used by Organix is not Tapentadol. It's the precursor --

THE COURT: I understand.

MR. CAPUANO: -- to Tapentadol. It's fully characterized. It comes with a certificate of analysis.

Plaintiffs took discovery of the company that provided that material to Organix. And so that material is understood, fully characterized and consistent with the product of Step 3 in the example 25 in the '737 patent. In the prior art patent --

THE COURT: Okay. When it comes with a certificate, what was the certificate saying?

MR. CAPUANO: It gives the identity of the material, its molecular formula. Dr. Hollingsworth knows, plaintiffs know how that material was made, what it is. And it's the same thing you get --

THE COURT: Does it recite the steps that were taken to generate it?

MR. CAPUANO: Not the certificate of analysis. It's just what it is. Plaintiffs took discovery on how it was made. We know how it was made. It's from -- we are still sealed in here? No.

THE COURT: No.

MR. CAPUANO: We know how it was made.

THE COURT: You can come back to it later, which is fine.

MR. CAPUANO: Thank you, your Honor.

THE COURT: Thank you.

MR.FITZPATRICK: So, just coming back to form A and form B and the fact that the form A is the more thermodynamically stable form, there are, in terms of looking

at this from an obviousness perspective, so, we contend that example 25, in practice, inherently anticipates the '364 patent. But, we also contend that it would have been obvious, the claims of the '364 would have been obvious and in view of a '737 patent.

And in terms of how a person of ordinary skill in the art would have approached that, a person of ordinary skill in the art would have looked at the '737 patent, and Professor Hollingsworth will explain, and would have seen that there are 20 some examples of specific molecules that were synthesized by the inventors of the '737 patent.

And so the person of ordinary skill in the art would have been focused on those, would have been motivated to look at those. They would not have started with the huge number of theoretical compounds but instead would have looked at what's the practical stuff. What did the inventors actually do? They would have focused on those. They would have been motivated to screen for different polymorphs of the substance.

So there's any number of motivations. But one motivation comes from the FDA itself. But in 1987, the FDA published guidelines where it says appropriate analytical procedures should be used to determine whether or not polymorphism occurs.

And so the FDA was saying find out if there are

polymorphs of your drug substance. Find out what they are. Figure it out. This is all routine stuff in this field.

And there are commercial reasons beyond the regulatory motivation. There are commercial reasons why this would be done. The techniques were well-known. They are routine. They are effective. Generally the most thermodynamically stable form is going to be preferred, for obvious reasons, because it insures that the drug substance won't convert to another form with different physical properties.

So, a person of ordinary skill in the art would have been motivated to look for different polymorphs, to screen for them and to identify the most stable one. And in doing that, given that this is a routine process in the field, they would have understood that they would have had a reasonable expectation of success in view of example 25 of the '737 patent. And so your Honor our evidence will show that the '364 patent also is invalid.

So your Honor at the conclusion of the trial, we will ask that your Honor determine that the asserted claims of the three patents are all invalid and that Actavis' product will not infringe the claims, asserted claims of the '130 patent.

THE COURT: Thank you very much. Much appreciated. Thank you.

Who do we have up next? Mr. Schuler, is a second set of slides? If you could just exchange those and take a moment.

MR. SCHULER: If I can approach, your Honor.

THE COURT: Yes. Thank you.

MR. SCHULER: And then while people take a minute, maybe a housekeeping matter. I plan to start with the '130 issue.

THE COURT: So do you want to --

MR. SCHULER: It might be easier to do it now.

THE COURT: That's fine. Mr. Schuler is going to start with the 130. He said perhaps this might a good time to clear the courtroom once again. So he can begin with that and then move on. But why don't you take a look at the slides first and we will determine that.

MR. SCHULER: More housekeeping, I will give you the best citation we have --

THE COURT: Go ahead. Hold on. Let me find my page. All right. Here it is B M. Vs. Teva. What's the cite?

MR. SCHULER: I don't have the cite yet but Federal Circuit Number 2013-1306. It was decided on June 12, 2014 by Judge Chen.

THE COURT: Thank you.

MR. SCHULER: And we will provide the actual

cite.

THE COURT: Thank you.

All right. My deputy is at the end of the courtroom. Let's see is everyone wants to turn around and see if they identify their folks and if there's anyone extraneous. Do you want me to do it informally or do you want to stand still? I will do it again just to make sure. Okay.

Let's have the folks from Depomed, please. Grunenthal. Actavis. Roxane, Alkem. All right. Counsel are all good with the folks who have stood up, I am assuming. Yes?

MR. SCHULER: Yes, your Honor.

THE COURT: No one has an issue. Okay. Let's seal the courtroom again. Thank you.

MR. SCHULER: Thank you, your Honor.

THE COURT: Everyone is getting a little exercise. It's late in the afternoon. It's fine. It's hot in the room.

MR. SCHULER: I may walk around a little.

THE COURT: We're trying to deal with the fact that it is super warm in this room. But it's unseasonably warm outside today so we are having a little bit of an issue.

(Whereupon the hearing is under seal)

(Whereupon the following takes place in open court)

MR. SITZMAN: Your Honor would it be possible to take a quick break at this point in time.

THE COURT: Certainly. Is this a good time? Let's take 5, 10 minutes. Is that good?

(Whereupon a short recess was taken.)

THE COURT: Let's continue.

MR. SCHULER: Your Honor, now I'm going to turn to the additional and independent invalidity defenses on the '593 reissue patent. You may hear it referred to in the course of the trial as the compound patent.

Those defenses are as follows: Lack of utility, self anticipation and obviousness, which is kind of an offshoot of utility that I will explain, lack of written description. With regard to three of the claims, those are the claims that are directed only to Tapentadol and then finally non enablement with regard to Claim 8 which is the broader claim that the Court inquired about earlier.

I now want to introduce the witnesses that will testify for the defense on these issues. You will hear from Dr. Jeffrey Mogil on Friday. Dr. Mogil is currently the E.P. Taylor Professor of Pain Studies at McGill university in Canada. He has an expertise in animal modeling associated with analgesia and pain. He also will testify as to the lack of utility and he will also testify about non enablement.

The Court will also hear from the defense through

Christian Wolf. Dr. Wolf is a professor of chemistry at Georgetown university. He is an expert in organic chemistry generally but he also has expertise in stereochemistry which is a subject the Court may recall from our claim construction process.

THE COURT: I do.

MR. SCHULER: Dr. Wolf will testify for the defense as to lack of written description, self anticipation and obviousness and lack of enablement.

I want to turn to what I think is the most straightforward defense which is lack of utility, which is under sections 101 and 112. And here are some of the precepts to kind of frame the issue for the court.

Initially there has to be some disclosure of substantial and practical utility for the invention. In addition, given the nature of the chemical arts, testing is often required to establish practical utility.

And the Federal Circuit has emphasized that to the extent that there are tests that are invoked they have to be reasonably indicative of the desired pharmacological response. I am going to come back in a minute to the reasonably indicative part of that. But for now I want to focus on the desired pharmacological response.

And again if we look at the legal backdrop juxtaposed against what is in the specification, Dr. Mogil

will explain that the desired pharmacological response here is the very first thing that the named inventor said about their invention in the summary of the invention.

What they said was that the underlying object of the present invention was to provide substances with an analgesic effect which are suitable for the treatment of severe pain without giving rise to the side effects which are typical of opioids.

And Dr. Mogil will explain that a person of ordinary skill in the art at the time would have understood this reference to the underlying object of the invention to constitute the desired pharmacological response. And you heard Mr. Sitzman echo that during his opening when he talked about the desire to have a compound free of these opioid side effects that he explained to you.

Dr. Mogil will also explain that with regard to the side effect aspect of the desired pharmacological response, there were in fact animal models that were in use as of the early 1990s to look for and evaluate whether an opioid compound was exhibiting these side effects.

But the evidence will show that the '593 patent specification contains no data from any such animal model relating to opioid side effects.

The only data comes from what is called the writhing assay which the evidence will show it has nothing

whatsoever to say about side effects. So, again, when we juxtapose the standard against the underlying object described in the specification and the limited data in the specification, there has to be data from testing that is reasonably indicative of the desired pharmacological response. But there simply is not with regard to opioid side effects.

So given the foregoing, we believe the evidence establishing lack of utility for this particular reason is both straightforward and clear and convincing.

Now the defense recognizes, your Honor that the plaintiffs assert that they believe that the relevant pharmacological activity is mere analgesia without the necessity of showing the absence of side effects. We disagree. But in any event the evidence will show that the specification does not demonstrate utility even examined under that lower standard and that is for two fundamental reasons. As.

Dr. Mogil will explain the first is that when we look at the specification, it contains data from only a single assay, the mouse writhing model. Here is part of the legal framework. Again there has to be a sufficient correlation between that test and the asserted pharmacological activity which is analgesia so as to convince those skilled in the art to a reasonable probability that the novel compound or compounds will exhibit that asserted pharmacological activity.

The question, your Honor is posed as a matter of science. It's posed to those who are people of skill in the art at the time of the invention. And so the question is was the mouse model on its own sufficient to convince those people in the field as of 1994 that the compounds tested in the specification had analgesia, which is the specified activity, or some other pharmacological potential activity. And as Dr. Mogil will explain, your Honor, the answer to that is a resounding no.

Let me step back and explain the mouse model a little bit. The mouse model works as follows: The mouse is given either like a saline control or it is given what is being tested for analgesic effect. A period of time elapses and then the mouse is administered something called phenyl quinone which is supposed to be a noxious stimulus that should make the mouse writhe. The technician compares the number of writhes that the mouse that got the test compound has versus the number of writhes exhibited in the group that was given the saline and there's a comparison.

Now, as the court will learn in the course of trial the patentees in the specification cited to a paper by some authors Hendershot and Forsaith regarding their use of a mouse model. Now the writhing assay is fairly old, your Honor. It's been around since the Fifties or even earlier. And this particular paper, as you can see, is dated from 1959.

This article itself which we have excerpted below notes that the model is subject to what is called a serious confounding effect, confounding means there can be an effect other than the one you're looking for that's causing the mouse not to writhe. Among other things, that might be sedation, the mice were simply getting tired or sleepy. It could be interference with the central nervous system which is called an anti colinergic (ph) effect or it could be interference with the Dopamine system which helps the neurotransmitters, that Mr. Sitzman mentioned, that helps regulation movement.

That wide spread knowledge among those in the field along with those deficiencies in the model led to significant criticism of the model well before the critical date of patent.

The Court will hear evidence that the criticisms were both far ranging, excuse me, wide ranging and consistent. The evidence will show the Court that there were a number of different criticisms like the lack of specificity, the confounding effects, but also the fact that the model may not actually be an innocuous stimulus at all that would mimic pain in a human being.

Here is excerpts from some of the literature that the Court will hear about, including literature, your Honor, that Dr. Mogil offered well outside the context and well before this litigation ever came to be.

Now the evidence will show your Honor that those in the field actually knew, and this is on the second quote here from a paper by Dr. Hammond at the university of Chicago dated from 1995, years before the prior art date that there was no model that predictable. No model that was used that would be widely predictive of analgesia.

And part of that, your Honor, is that unlike other pharmacological responses which might be reflected in a simple invitro assay where you have a receptor that there is some binding activity to, the evidence will show that pain is a multi-faceted experience. That goes beyond mere simplistic binding to a particular receptor.

So, as Dr. Hammond wrote here, people in the field at the time understood that the only way that you could have what she says is an inference of pain and its modulation in animals was only through what she determined as judicious use of complementary models plural of nociception and assessment of motor function. And by that means is the mouse actually simply not being able to move or is there true pain relief.

Notably plaintiff's expert on this issue Dr. Ossipof (ph) conducted his research in the field consistent with these precepts and with Dr. Mogil's opinions on that subject. And as we've all heard throughout the course of our lives, your Honor, actions speak louder than words.

Now, the second fundamental attribute of lack of

utility is that there are three claims, as the Court heard earlier from Mr. Sitzman, they directed to Tapentadol molecule. But, when we look at the data in the patent, there is no data for example 25 which the Court has now repeatedly heard is the one that supposedly refers to Tapentadol.

So when we go back to the legal framework, there's supposed to be test data to convince somebody in the field to a reasonable probability that the novel compound has the asserted activity here. The sole novel compound ostensibly of these three claims is Tapentadol but there's no data for Tapentadol.

Now the evidence will show that the plaintiffs eventually did attempt to submit data for Tapentadol on two separate occasions. But the evidence will show several things, the first is the test data for Tapentadol was submitted after the filing date. Plaintiffs contend that one such submission occurred when Dr. Buschmann submitted a declaration to the patent office. But the evidence revealed some ambiguity on that score.

In the text of his declaration he mentions example 24 but that's not Tapentadol. And then in the table there is a mention of example 25 but there's some confusion there. The evidence will also show that there's no indicia submitted by Dr. Buschmann that the data that he was submitting was available as to the priority date. The other data was submitted in the year 2005, your Honor, in connection with the

reissue application. But that was 11 years after the asserted priority date.

Given the foregoing, the evidence will show that the plaintiffs' invocation of the data submitted during prosecution is not legally pertinent for two independent reasons, initially as Judge Coe (ph) who has been handling the high profile Apple v. Samsung matters, recently emphasized, courts cannot look at post filing test results as evidence to substantiate utility which is frozen in time as of the asserted priority date.

Here there was no, again no evidence submitted to the Patent Office that any of the information concerning Tapentadol as a molecule was available as of the filing date. In fact, the evidence shows that a number of the data sheets that were submitted in the reissue process bear dates that are well after the priority date, some as late as 1999.

The second problem for the plaintiffs is that we challenge priority. And the limited exception for looking at post filing data doesn't apply but only applies when priority is not at issue. And here are our excerpts from the caselaw in that regard.

Now, you may hear a suggestion during the course of trial from one or more of the plaintiffs' witnesses that one could infer the activity of Tapentadol because there's no data for Tapentadol from the activity of other compounds that are

in the table. But, that theory suffers both legally and factually.

Legally, the caselaw talking about looking to the activity of other compounds is in the context of prior art compounds. And it's limited to those for which there is structural similarity between the prior art compounds and the compound of the count.

Now, Mr. Sitzman just got through explaining that plaintiffs do not believe there are structural similarities between Tapentadol and any of the prior art compounds. But, to the extent that the plaintiffs produce any evidence of that, that has obvious invocations for other invalidity defenses.

But, more importantly, perhaps is that factually the evidence will show that people in the field, the scientists would not presume that a different enantiomer would be active for a variety of reasons which include the fact that the receptors we are talking about have a particularized three dimensional shape for accepting the molecule. And the evidence will show that when they are tested in the same assay, enantiomers typically have markedly different activities.

Now, I want to turn to the other aspect of the utility which is the self anticipation and obviousness. And that defense invalidates the asserted claims even in the scenario the Court accepts and evaluates the evidence submitted during the prosecution regarding additional data or potential

activity.

In essence the evidence will show, as I just previewed from Dr. Mogil, that the claims, the specification does not support the claims, the priority date. And that again is for the two fundamental reasons we don't have any data for Tapentadol which is the sole subject of three of the four claims. And the only other claim, claim 8 is supported only by the writhing model, which is what we saw, no model was deemed itself reliably predictive as of 1994.

Now, the evidence will show that the applicants implicitly acknowledge the shortcomings in the specification by submitting about 80 some pages of data sheets from animal testing models during the reissue process.

The evidence will show that that did not occur, however, until 2005. In the interim there was a public disclosure of Tapentadol and its efficacy as an analgesic agent. So before the patentees could establish utility in 2005, there had been a sufficient public disclosure of Tapentadol, its structure and its analgesic activity that would invalidate the claims for lack of novelty.

That's precisely what happened. I'm sorry, this is actually played out before your Honor. This is a scenario that's happened in the course of events where a patentee had filed a patent application but lacks sufficient information to support utility.

They subsequently try and put in information that would support utility, but, in the meantime there has been public disclosure of information that is sufficient to invalidate it. And that's precisely what happened here.

Dr. Mogil will explain that the specification lacks data for Tapentadol or for any other compound that will be sufficient to show analgesic activity. And so Dr. Mogil will testify that the first time that the patentee submitted data that may have been, that was sufficient from multiple animal models to show some activity for Tapentadol and the other compound was in 2005.

And of course your Honor just to stop here for a second, again you will see dates on some of these pages from 1995, 1996, 1999. So, those axiomatically cannot go back and retroactively support utility as of 1994. Because as you can see on the face of them, they didn't exist.

But what happened is also, your Honor, a paradigmatic example of actions speaking louder than words. We believe that you will hear at least once in the course of trial from a witness for the plaintiff who will say that the data in the specification actually is sufficient to support utility. But if that's the case then why submit this data at all.

You will not hear any explanation for that action during the trial because that is, that submission came from Dr. Strassberger and Dr. Strassberger is not being called by the

plaintiffs to explain his actions.

The evidence will show that Grunenthal's action logically is consistent with the conclusion that they acknowledge that a person of skill in the art would not regard it, would not have regarded the data in the specification as sufficient.

So again what happened in the interim 11 years between 1994 and 2005 well, one reference that had published on Tapentadol is from the WHO, the world health organization's drug information guide from 2002. And you can see we have the popular name Tapentadol. We have the chemical formal name for Tapentadol. We have it's same structure and it's a description that's it's analgesic.

Dr. Wolf will testify that a person of ordinary skill in the art could have used the information to readily synthesize Tapentadol. And Dr. Mogil corroborates that you quickly verify that it had analgesic activity. That disclosure then invalidates or renders obvious all of the asserted claims.

Your Honor may have asked a question or there may have been a suggestion by Mr. Sitzman how would you ever go through and select Tapentadol out of those thousands.

THE COURT: I did.

MR. SCHULER: Here's the reason. The priority date for the polymorph patent I believe is 2004. But as of 2002, it was known that this is the one that's an analgesic and

has enough activity to place it in the World Health Organization's drug information guide.

Now written description, this is limit --

THE COURT: In terms of the family of those using it, this is the only one that showed up in the World Health Organization's document?

MR. SCHULER: To our knowledge this is the only compound out of those I will say.

THE COURT: And I refer to it as the family.

MR. SCHULER: I will admit that it's a family and I will admit that it's millions.

THE COURT: Okay.

MR. SCHULER: We will come to that in a minute.

THE COURT: Okay.

MR. SCHULER: Lack of written description is confined to those three claims that are limited to Tapentadol. The evidence will show that the underlying patent application specification fails to adequately describe those claims. And Dr. Wolf will testify for the defense on this issue.

Briefly the standard, the burden we bear. We have to show that the specification does not reasonably convey to those skilled in the art as of the filing date that they possess Tapentadol. We note however your Honor it's an objective inquiry. You have to look at all four corners of the specification and you have to do so from the perspective of the

person with skill in the art.

And those precepts are important for two reasons, initially their claim for written description, I believe you will hear, is effectively well we had a structure and we had a synthetic route. That's enough. But remember you have to look at all of the four corners, not just a self-serving subset of that information.

In addition, the evidence will show your Honor that the chemical name in the original application is indisputably not Tapentadol. And of course you have to look at all four corners of that information in the specification.

Now the evidence will also show your Honor that when the patentees attempted to correct the name, they still corrected it to a 1R 2S configuration. That is not Tapentadol. And more significantly when they submitted that correction they said that the supports for the amendment was found in the original formula, which Dr. Wolf will explain would mean they are conveying to a person of ordinary skill in the art that they convey the new corrected name now conforms to the structure that the plaintiffs are pointing to as evidence of written description.

And Dr. Wolf will explain when you have contradictory information like that, a person of ordinary skill in the art would expect to see something more than just a structure. A person of ordinary skill in the art in chemistry

would have expected to see information confirming testing that had shown the actual structure.

The evidence will corroborate Dr. Wolf's testimony in several ways including evidence showing that the applicants themselves, your Honor, did not know at the time of the claimed priority date, whether or not they had synthesized the compound having the requisite 1R 2R confirmation that is associated with what we know today as Tapentadol.

There's some additional legal guidance we think is pertinent and that is that the adequacy of the written description varies with the context. And it depends on the complexity and the predictability of the relevant technology. And you will hear from the plaintiffs themselves that chemical arts are unpredictable and you can't predict necessarily the activity of compounds.

But the evidence will show that it's also unpredictable from the synthetic side. That you don't necessarily synthesize what you set out to synthesize. And the final precept is that it changes with progress in the field. It may have been the case in the 1960s that publishing a structure might have been sufficient to show somebody that you had thought of a compound. But, by the mid-1990, Dr. Wolf will explain, a scientist would expect to see data, analytical data of the sort that would confirm the structure.

The evidence will show that the little data that

is in the patent specification which is melting point and optical rotation, there is no data from the structural technique like nuclear magnetic resonance or N.M.R.

The evidence will further show that the only data that's here, the melting point, the optical rotation says nothing about the structure. The evidence will show that the compounds examples 24 and 25 are supposed to be enantiomeric. As the court may recall, enantiomers are non superimposable mirror images like my left hand and my right hand. And they are supposed to have an enantiomeric relationship.

But the data, Dr. Wolf will tell you, does not show an enantiomeric relationship. They should have the same melting point and they do not. They should rotate plain polarized light in equal but opposite directions and they do not.

Dr. Wolf will explain why that data has a bearing upon whether the applicants actually possessed Tapentadol at the time.

Now, I'll move to the final issue which is non enablement of claim 8 and this will be brief because the facts, your Honor, are effectively undisputed. Dr. Wolf and Dr. Mogil will each offer testimony on the non enablement defense.

The legal precepts are very straightforward. We bear the burden of showing that one could not practice the full scope of Claim 8 without undue experimentation. But the

Federal Circuit has offered some additional guidance which is that even where the experiment is routine, if there is a whole lot of routine experimentation, that can still be undue. And that's from the Wyeth versus Abbott case.

And here we have Claim 8 your Honor. And Mr. Sitzman got it absolutely right, Dr. Wolf did calculate the number of compounds that could be used in this method and he calculated a huge number. It's numbers in the millions. And that's accounting for actually all of the potential physiologically acceptable salts that one could make.

But let's call, just call it one million compounds. Dr. Wolf will testify that practicing the full scope or both Dr. Wolf and Dr. Mogil combined will testify that practicing the full scope of that claim will take many, many years of experimentation. Given the unpredictability of the chemical arts, Dr. Wolf, I'm sorry, evidence will show that the only way that you could determine which of the compounds would be suitable to treat a mammal suffering from pain, which is the subject of the method, is to first synthesize that compound and then test it in one or more animal models or multiple animal models to see if it had analgesic effect.

The evidence, in fact, will show your Honor that in the course of the Tramadol project that Mr. Sitzman talked, about nearly half of the compounds that they had tested were found to have no efficacy at all. Dr. Wolf will explain that

while the chemistry is fairly straightforward, it would still take on average about one day to synthesize each of the compounds. And we don't anticipate any material dispute between the experts on that issue. And so right there we have a million days.

And Dr. Mogil will testify that completing a couple of animal assays to see whether the compound has that activity would take about another day. So right now we are looking at 2 million days, which is about 5,000 years.

Now, final slide. In that sense Claim 8 is eerily reminiscent of the claims that were invalidated by the Federal Circuit in the Wyeth case. There the representative claims likewise recited a method of treatment using a class of compounds. There they were called Rapamycin compounds.

The Federal Circuit explained that practicing the full scope of the claims would require synthesizing and screening each of at least tens of thousands of compounds.

And they said given that circumstance, the resulting need to engage in such systematic screening for each of the many Rapamycin candidate compounds is excessive experimentation.

Now you heard Mr. Sitzman say the exact opposite during his direct, that it doesn't matter, that you wouldn't have to synthesize each of the compounds as a matter of law. We beg to differ. We think the federal circuit has

specifically ruled that to practice the full scope of claims like this would require synthesizing and screening each of them.

And there's no dispute your Honor that when you do so with regard to Claim 8, you are talking thousands of years. That concludes my presentation.

THE COURT: Thank you very much. Much appreciated. I think we are on our last leg of the defendants' presentation.

MR. ALY: Yes, we are.

THE COURT: All right. You can exchange the slides. Take a look. Let me know if there's any difficulty with them.

MR. ALY: WE did at the last break. I am advised there are no difficulties and I can approach with the presentation.

THE COURT: Yes. Thank you.

MR. ALY: May it please the Court.

THE COURT: Yes, please begin. Thank you.

MR. ALY: I'm Imron Aly and I have the honor of representing Alkem laboratories, the third and final defendant today. And representing Alkem their managing director came from India and I'd like to introduce Mr. Sindeep Singh (ph) who is here in the audience with us today.

THE COURT: Thank you. Welcome.

MR. SINGH: Thank you, your Honor.

MR. ALY: Your Honor, we have a different backdrop and then we are going to address the same patents but focus on different issues than the other defendants, not because we disagreed with what they said, but obviously because we want to focus on issues that we will be presenting until your Honor gets a complete picture of the different issues without hearing the same thing.

THE COURT: That would be fine. Go ahead.

MR. ALY: Slide two is explaining our backdrop and the story starts where Mr. Sitzman's story started with Tramadol. Tramadol is actually something that was inventive. It was something that helped people and it is something that had a patent on it.

But what happens at these pharmaceutical companies your Honor is delay. Why they have an incentive your Honor to keep generics off the market as long as possible, some people call that evergreening in publications, other people call it life cycle management.

But the business strategy remains the same. You come up with something, keep trying to tweak it to do something else. So the patent life cycle can continue indefinitely . That's what happened here. Look at the timeline. We got the compound application filed in 1994 which included not just Tapentadol but millions of other compounds as we just heard.

Why? Because it was a place holder.

Several years later after they finally found out that Tapentadol is the one they want to focus upon, then they do an activity test in 1997 and submit that to the Patent Office, that's the late data about example 25 in Tapentadol that they are focusing upon.

* and then in 2003 they do a reissue application changing the claims and saying let's not have just the eight claims that we originally submitted, let's add over a hundred brand new claims some of which focus on Tapentadol.

That's the timeline for how Tapentadol came to be in your Honor asked what happened with the reissue application I intend to address that when I show those slides. But what happened in a nutshell is Grunenthal did not have Tapentadol at first in the patent and later in the reissue put Tapentadol in it. That's what happened.

While these patents were being processed, what about the other two patents. The other two patents support this theme of delay. In 199.

THE COURT: When you say it wasn't in the reissue and then it was the issue.

MR. ALY: It wasn't this the original patent.

THE COURT: In 1994 though if we are looking at Tapentadol and other compounds correct.

MR. ALY: That's what the patent says but it's

not Tapentadol included that's what the plaintiff says pardon me but Tapentadol is not included but of some typos that were in there is what plaintiffs call them we call them the wrong stereochemistry and the reasoning here is remember the four compounds that Mr. Sitzman identified there is an example 25 that's the example we've all been talking a lot about and will continue to do so and on that example stereochemistry is admitted wrong.

So somebody reading that application in 1994 until the reissue application 2003 only really know for sure what compound that wasn't.

Now plaintiffs want to have it both ways and say yes they would know what it was at that time but also no one else could be able to replicate it during the polymorph test because they wouldn't know what compound they are make g and I'm going on be addressing all of to e patents and about but plaintiff can't have the both ways is another key part of our presentation.

In that compound and then we they submitted reissue in 2003 they told the Patent Office don't worry we have the figure here so the figure supports the change to the supposed typo.

The problem from a legal point of view is there's two things that are inconsistent the figure and the nomenclature the numbers or the letters assigned to it so which

do you pick. That's why there wasn't support in the compounds application and they had to do the reissue and then they added over a hundred other claims.

While that was going on internally they were doing polymorph tests on say what polymorph do we have here. In 1998 this is an internal test which he will eye show you where Tapentadol was tested for a polymorph and by 1998 they had Tapentadol in its form A low and bow hold it's form A because it stable formulated method you get if you make Tapentadol you get form A and they just did nothing with that information until 2004 when they filed an application for the Tapentadol polymorph patent at issue here:

Why would a company sit on its hands for six years if they had invented something it's because they didn't invent anything. They had form A in their pockets. They waited six years and then filed a patent application for it.

And your Honor Mr. Sitzman said well at that time we didn't have our own lab. We didn't have an ability to test the polymorph. That's not the standard of obviousness that you didn't have a device to do the test in your lab and in fact the 1998 test before they had the lab, they sourced it out. They sent it to a lab. Just like we would for an a blood test sends it to lab see was e there and what do you get back form A.

The third and final patent the '130 is the

Tramadol history applies here as well. In 1998 or the oh Mack kneel working with Janssen the former plaintiff in this case the one who sold the product to Depomed, in 1998, published that Tramadol works for polyneuropathic pain and particularly the diabetic polyneuropathy.

What happened there Tapentadol existed but plaintiffs just decided let's not bother trying it out for the neuropathic pain for years because what happened if you do that you get a longer patent term at the end of the day 2007 is when they finally applied for polyneuropathic pain indication and Mr. Sitzman identifies that the submission included some FDA data that they later obtained some Phase 3 testing.

This is going to be a key issue that Phase 3 testing is for what somebody can put on their label. You can't market something on the label without at least the Phase 3 testing Mr. Sitzman said that we agree. But that's different than a patent standard for were whether somebody invent a patent and say I take credit for invention for using social security they basically the same drug as Tramadol with some tweaks to it and then saying it work for the same thing.

It's not that it works for a new indication it didn't solve any new problem that's why when we are looking the he can approximation part at issue on you slide 3 which everybody has used it but I tweak, I want to add to is following that we e having been evergreening problems what

naturally happens by definition is the later patents at you later they get weaker and we're there's just have there's not much left to tweak or not much left to refine social security that's what happened here.

What happened in 2022 the compound transition patent where e changed some things on the patent and say here is brand new compound the 2025 that's patent that expired but for the polymorph and 2028 that's the compound expires are to method what I'm showing you an example hire that if plaintiffs were to succeed in showing that the first patent is not invalid but we succeed on showing that the second two patents are invalid then there's product launch in 2022.

If defendants can show that all three patents are invalid then we can launch the day that the decision is rendered because it would be all invalid.

Next slide four to talk about what Alkem is going to do about that it's I a company from an India but also has an office in Montvale, New Jersey. They have done their research and development oncoming up with this formulation they have purchased and have plants manufacturing facility in the U.S. and really working towards developing this product so that there's generic version of Tapentadol available to the public.

Here are the claims representative claims that are being asserted for the '593 patent, '364 patent and '130 patent. You've seen these representative claims but I will go

into this in a little more detail for right now I want to explain that the standard of invalidity is because we are contending all three patens are invalid.

The standard for invalidity is would it be obvious to a person of ordinary skill in the art. And what is that person in ordinary skill in the art it's not just an average lay person it's actually somebody who knows what they are talking about in that field and the parties have agreed upon generally the definition is and so when we're looking at eat from from perspective there's another very unique attribute to an ordinary person of skill in the art hypothetical person that is doesn't apply to any real human being and that is they are deemed to know every prior art reference in their field. Deemed to know it.

So it's hypothetical test for the following reasons the question presented is not did an inventor subjectively believe they were doing something new because they couldn't possibly have known all of the prior art.

The question is would a hypothetical question of ordinary skill in the art have believed that it obvious in view of what is was available the all of the prior art and that's important because what patents are awarded for is advances on the technology and not just baby steps not just regurgitating what the art had already taught even if the inventors themselves didn't realize that.

For the compound patent therefore we are having Dr. Prisinzano addressed what is specialty is making drugs synthesizing drugs specifically for pain and he will explain to you why the modifications from Tramadol to Tapentadol were obvious.

For the method claims Dr. Buvanendran all three defendants have talked about him will explain to you why that's obvious and the polymorph especially in view of the Tramadol and other patents that exist on Tapentadol and polymorph wise we have Dr. Steed who will take a look at and explain the prior art and why the prior art when you follow the recipe of the prior art you get form A which is the same thing that Grunenthal evidence shows.

Most of my time your Honor will be spent on that polymorph patent but I do want to address the other two the Alkem perspective.

THE COURT: Go ahead.

MR. ALY: On slide eight I wanted to point out what literally hand in the reissue this is original patent so we doctrine the original patent law where if there's something in the original patent that specifically and distinctly set out as a separate inventions' that's what you can claim in reissue reissue are by law something where you can say you know what oops I forgot to claim something but you can see it's right therein the patent that's legal.

What's not legal is saying take this particular place holder with millions of combinations and then now go and cherry pick or change those compounds themselves and then say I want to pick one of those going forward that's the original patent rule.

What happened here is this reissue that occurred of the original patent that's '737 then we come reissued as '593 and as Mr. Sitzman said we look at the same specification but the difference is the difference is now we have some claims that are going to be in Italics. As I'm going to slide ten.

And slide ten is showing the italics any italicized claim in a reissue is a brand new claim. It didn't exist before so all of these e new claims including 117 which is specifically about Tapentadol with all the numbers and the letters correct in claim 117.

Now when I ask explain what was disclosed in the patent in example 25 as far as the errors are concerned we don't have to look very far. The 539 patent one the things with the reissue is you have to change in brackets what was changed basically to put in Italics was removed adds what changed and you get the 1R 2R. Or the 1S 2S or particular examples here that changed overtime and these the change from the original patent over to the reissued patent but that's the change that shows if steer chemistry is so important as Mr. Sitzman has explained and argued in that case then we have to

hold them to their own standard and say you have to have gotten that right and you can't cherry pick those later.

I think my colleagues addressed example 25 wasn't tested so let me conclude the '593 portion by saying that there are core and none core elements that were known in Prisinzano will explain that there's a pharmacophore word which basically means the core the guts of the compound the thing that does the work and then there's other parts of it that we can tweak and we can see what happens if those are changed.

The analogy and I'm not going to go into all the details of '593 as Mr. Fitzpatrick has covered the changes but analogy that I wanted to make sure to explain there's got to be some rational basis to do what you're doing.

What would person of ordinary skill the art change are or not change and why that's the discussion or obviousness and just like as an airplane some of the things you're not going to change. And other of the things you might depending on the application.

Here's an example you can't really change the fact of having an engine or a wing. You can change the windows maybe you don't need them maybe you need a bigger one maybe you need a smaller one the tips of the swings maybe you need speed maybe you need fuel efficiency. These are the things, I am not a person who designs airplanes, but a person who designs airplanes would know these things you don't change. These

things you can change.

If it's within that field, it's obvious they are doing something completely different than expected and never before taught in the literature that's different story but here the defendants will show with literature why we're doing each of these change to the compound and why that would be obvious.

That's my portion of the '593. The '130 patent the method claim here the issue is the following on claim 15 I'm sorry slide 15 claim one the '130 patent has this method of treat polyneuropathic pain and the question is is polyneuropathic pain covered within the word pain. And we originally thought that no it's not.

And I'm going to slide 17 to say we originally thought well we don't know if it is or isn't than a that was disputed because the plaintiffs attorneys and the plaintiff's experts had originally said when you are looking at pain if it's in the prior art because we had the invalidity argument and if the prior art just says pain. That isn't enough. It doesn't have what I'm now going to call the magic words analysis the magic words analysis is does eat say neuropathic pain in particular or does it say pain in general.

And the argument plaintiffs had before there were some changes in the case and just before the evolution of the case let me put it that way is a the case evolved the plaintiffs have changed their position to the prior art to

invalidate too specifically use the magic words and now at trial it's pain includes neuropathic pain.

It's change and reacting to that change if you look at Alkem label on slide 18 there are two indications, the first moderate to severe chronic pain in adult and the second is neuropathic pain associated with diabetic peripheral in your. And the question from an infringement and invalidity points of view is actually the same. If I may approach the screen your Honor.

THE COURT: Yes go ahead.

MR. ALY: If the two indications the seconds one is the one that plaintiffs have accused of infringement. But if the first one here its also infringing which we ask their experts about if that's also covered by the claim just having severe chronic pain then includes the neuropathic pain, then that's the invalidity or infringement choice.

Plaintiffs can't have the both ways. Either there's infringement or there's invalidity and they can't have the both ways. Why is that? Because the prior art taught using Tapentadol in particular foresee veer pain. Here's an example of prior art and it's Dr. Buschmann should be Dr. Buschmann himself 558 patent but already published that you can use and if that fore severe pain it's already out there.

So if that general reference to pain without the magic words polyneuropathic pain includes polyneuropathic pain

then this disclosure of severe pain is invalidating as anticipatory it anticipates it anticipates.

There's other anticipation as well and your Honor asked about the Tzchentke references and we are waiting to see what plaintiffs have to say about Dr. Tzchentke the following reason Mr. Sitzman satisfied two things, Dr. Tzchentke is employed by Grunenthal Janssen and that he was part of the team that helped develop or worked on this compound what Mr. Sitzman left off Tzchentke is not on the patent he is not an inventor so we hat Tzchentke one Tzchentke one Tzchentke two Tzchentke three why is he writing all of these articles where they file author that are patent application did he not think it was an invention did he not know what was being done internally, why is he doing these publications.

Now the standard for the critical data and this is issue that really is remaining, by the way Mr. Sitzman used a brand new divide initial of critical is he not the one I'm familiar the one I'm familiar you take the application 2007 here, you subtract one year March 2006 and it basically means anything before March 2006 is automatically prior art and if it's within the window of 2006 and 2007 which it is here then you have to figure out if it's prior art or not based on the testimony of the plaintiffs.

The burden actually shifts to the plaintiff to say I see it's before March 2007 when we applied for our patent on

this method claim but maybe we have evidence to show that we published parts of it or we published something that is already including of the invention.

And it's only because of the inventors work instead of somebody else's guess what Dr. Tzchentke is one of the witnesses they only wanted to have by deposition and in that deposition which we will again submit after trial he says he did offer additional materials in that article that were not provided to him by the inventors and that makes sense he wrote the articles.

Also on this method claim we have obviousness type double patenting which is that going back to our famous '593 patent event which is asserted or the '737 from which with derives again it's the same thing. Originally they had pain in there pain was already in there and so if pain is enough to automatically include neuropathic pain which is plaintiff's position, then by that definition they've already got a patent on eat and they don't deserve two patents on the same thing with differ rent expiration dates.

Obviousness also in that Tramadol did do the same thing and Mr. Fitzpatrick hints had on this it was well-known in 1998 Tramadol was tested for diabetic in your operate I in particular and the conclusion was yes it works. So the invention here is take the derivative of Tramadol waits nine years patent it on the same exact thing. We don't believe

that deserves a patent either.

Slide two summarizes why because the known characteristics between the two drugs and the conclusion that it can also be doctored. DPN therefore we believe is the obvious one.

Now I'm at '364 patent slide 25 which I would like to spends the fall balance of the time. '364 patent has claims to a new crystalline form and claim 26 or slide 26 claim one I should say has where the claim is recited.

I just want to take a little bit of time here because I am building up to a slide where I'm going to spend a lot of time. Little bit of time here is when we talking about polymorphs what are they and how do you know you have one what are they is crystal patterns within a solid structure and so if you have a chemical and you put it in solution you stir it around. There's no, there's no crystals yet.

You've got it in solution for example if you dissolve salt our you can dissolve sugar you've got a solution then you do certain steps to see if you can extract out the solids and make crystal out of that you get sugar crystal or salt crystals that just as a general analogy when you get out those crystals at the end of day threes what you measuring to see okay are these crystals that was their shape and Mr. Sitzman put up a slide with 7 or 8 known shapes and just a beauty of nature is these shapes can be triangles, rectangles,

squares, rhombuses from Geometry.

And it doesn't really matter all of the time it doesn't much of the time is it doesn't matter here how do you it's a got one of the particular forms you do an xray defractogram. You put it through a machine and it gives you peak numbers about where you see little peaks that's the technology it's not a new technology it's not one that Grunenthal had invented.

And when you look at slide 27 then this is showing you the result of the two forms that exist for Tapentadol. There are only two forms that exist for Tapentadol only two. Form A and form B and looking at the peaks I can't make much of this but the experts can look at an eyeball and it says yeah it looks like a lot of over loop its look likes there's a very similar structure but here's what structures actually look like when you put them together and it's slide 28 which is these are given different names monoclinic or orthorhombic.

But all it really means is you got a rectangle and a slightly leaning rectangle that's essentially what you have here the two forms form A and form B the claims just say form A the claims. Do not have purity requirements much there is no purity requirement this the claims. So as a result it's not a claim that says 99 percent pure form A or more. This is just form A. Do you see it yes or no.

And for that reason even combinations of form A

and B are included within the claim and would anticipate if found in the prior art and that won't be disputed.

Internally at Grunenthal they had done the test themselves slide 29 shows the form A and form B the rectangle and the slightly leaning rectangle that's what they found.

'364 patent then says and this was again filed in 2000.

THE COURT: I am sorry go back to slide 29 what are you saying that shows.

MR. ALY: Slide 29 is showing this is Grunenthal internal assessment conclusion about what are the forms of Tapentadol and they are saying form A and form B and it's rectangle and the slightly leaning rectangle and form A is the one that's in the patent.

THE COURT: Conclusions from which substance.

MR. ALY: Tapentadol.

THE COURT: I understood but do we know what batch or what I what is this from.

MR. ALY: This is a synthesis of a lot of different testing I'm going to show you the test report in a moment it's lot of different testing that was done by an outside vents or and synthesize of in an update that's provided here here ear the two forms and what I know about them so in the particular analysis it's not a matter of saying here you have to use this particular method to get A or this particular

method to bet.

The issue that was presented here was if I sent it to a lab and they do whatever they want with it what the the different forms that they get and the answer was here's your two choices.

THE COURT: Do you know what they sent.

MR. ALY: To that lab.

THE COURT: Yes.

MR. ALY: That lab they sent originally form A Tapentadol and that's actually going to be part of the unclean hands issue that's coming up which is they sent form A Tapentadol and the company messed around with it and said the different tests sometimes they got form A and sometimes they got mixtures of form A and B and then they put a patent application after that saying to the patent office hey we gave the a lab form B which which was incorrect which gave the lab form B and we got back form A look we should get a patent on this.

But in reality they gave the lab form A and got back form A and said we should get a patent on this. That's what the evidence will show.

THE COURT: What is the evidence you're going to use to show that they actually gave form A as opposed to form B which you are saying they said they gave.

MR. ALY: The Grunenthal reports. They have

internal SSCI reports the SSCI by the way is the company in Indiana that did the testing they document what they received and what they did with form A was so unstable it was really hard to work with.

It's very difficult to keep it stable at room temperature and for that reason form A.

THE COURT: I know we are going to hear from the witness but are you saying that the report itself represents what form was actually sent to be tested.

MR. ALY: It does.

THE COURT: And you're saying it rents that its sent form A to be tested.

MR. ALY: It does.

THE COURT: Form A resulted in an analysis which showed form A and form B present.

MR. ALY: After they did different tests in between so the test that was given to S SC A was task. Here is form A Tapentadol and you should do different recrystallization with and see what form you get out if I may here take short time out to explain something.

THE COURT: I am not sure what recrystallization is.

MR. ALY: That is what I was going to explain. You've got something that starting material that's crystal and then but all that matters is that you know what you started

with when you are doing the crystallization procedure so if you have something you say here I got in something. I know it's this compounds recrystallization now put it in liquid mix it up. So now it's in a solution. It doesn't have a crystal anymore.

It's like know flakes stirring them into the pot you lose all the crystal then you do techniques to put it back in on crystal form which the in snow make might be freezing it or putting it through a tube. I am not sure but there are techniques too be used to get a crystal back out that's recrystallization if the middle step you to take the pot and you add different ingredients or add different conditions. The goal is to see do I get anything in a different shape a rhombus were this, do I get a square at the time that's test that we are talking about.

Recrystallization is important because the Step 1 2 3 4 analysis that we need to address.

THE COURT: I'm sorry, did you say this was done solely pursuant with the recrystallization or some of the tests were crystallization.

MR. ALY: All SSCI tests for recrystallization. Other tests that Grunenthal did internally that were not all recrystallization so they were making different types of products internally to see what formed the synthetic process.

THE COURT: I'm sorry with respect to slide 29 is

the only through recrystallization or is this the one that's both.

MR. ALY: You know I would think it's only recrystallization because SSCI got a solid product to start with but then internal work that they did Grunenthal had the same results that these are the only two forms that they could ever find as well A and B.

THE COURT: I'm sure we will hear more on it thank you.

MR. ALY: When that's what we are interested in talking about. I said that the two forms don't make a difference and I wanted to point to the admission in the '364 patent itself that says that so we don't have to go very far the polymorph patent is telling us crystalline form A is the same pharmacological activity as form B but is more stable under ambient conditions.

So the important thing here is you too take either form A or B give it to somebody it would have the same effect and that's what the FDA is really concerned about and that's were e polymorphs if they ever matter matter when you get form A to somebody that helps their pain you give forms B to somebody and that doesn't make a difference but you better be pretty sure what you're given if that's the situation. This is not that situation.

This situation is you could give form A you could

give form about it really doesn't matter why would you pick form A. It's because it more stable under ambient conditions.

All the reports that Grunenthal got /TPWR third parties said you knee I'm having a tough time making form B but if I cook it to above 50 C which is about '130 degrees Farenheit if I took it to that number or higher I'm starting to see form B yeah.

But guess what that doesn't matter who is going to be '130 C for manufacturing conditions they are not that's why from Alkem's points of view we infringe because everybody should be using form A that's the room temperature Table 1 that's the one you get when you just sitting there making it in a lab.

As to the question as well on utility defendants have expert Dr. Metzgar who will address the point and say when I'm looking the a statement in '364 patent even as to the claim that B is more stable, even that there's no data in the patent so they are making the claim but where's the data for it that's a question that will be addressed by Dr. Metzgar.

Now we get to the prior art or polymorphs and so that if u follow the rest pie of the '593 patent which was the one that that they applied for in 94 you get to the form A or mixtures of the form A and B which is good enough in the '364 patent.

How do I explain this. This is the slide 33

where I will slow down for a minute and then take sometime to talk about. The reason is as follows: Mr. Sitzman talked about steps 1,2, 3,4 because example 24 which is in this prior art '593 or '737 has what they are calling first step and second step a third step and then example 25 is where Tapentadol comes into the picture with the right steer chemistry with a fourth step.

I don't know if these are the four steps that the plaintiffs are now tracking because this is the first time I saw the 1, 2, 3, 4 numbering. But here's what I do know. That the example 24 third step, that's where the crystallization happens.

Here I'm reading from column 18 line 64.4. 3 grams of plus 23 from Step 2 were added to one milliliter of concentrated hydrobromic acid why is that important why am I reading that it's because the third step starts with a solid then they put it into a solution and then they do the steps in the example to see what crystals form.

So when Mr. Sitzman said well what about the first step the seek step where things were happening to the chemical structures and the chemistry was being developed overtime, doesn't matter. Doesn't matter. And your Honor when we had the call about ma Rita Mueller' work the reason there's so important is this is the critical question.

Do I have 4.3 milligrams of plus 23 from Step 2

that's the starting point of this crystallization project there's other starting points we agree to get to that point. But you better end up at that points and that's when you need to check and stop and say do I have this. That's what the defendant's expert did, we hired them.

The University of Wisconsin is who we hired. They got something that they purchased and they said is the this plus 23. They did a test do it NMR and says yes that's what it is for sure. So that's where they start with.

Now contrast that with the evidence that plaintiffs will put on where they don't have that evidence because they are saying don't worry about it we made the chemistry the right way from the whole step earlier from making the right compounds so we don't have to check our work and show you that the N. M. R shows that for the Line 63 compound which is the plus 23 that's the compound that has the structure to it.

We don't have to show you that there's what plaintiffs are saying and these why Marita Mueller we think is not here because we asked her about these things we are going to talk about the particular evidence and testimony she presented in the next slides for rights now we're saying one key step to make sure are you doing the crystallization properly or not is you start right there is my starting material correct.

You take that starting material, and that put it into the solution and then you put it into this crystallization thing then you finally do the X R D to see if did you really get the right form A what form did you get that's why I want to spend a lot of time on.

THE COURT: Go back to the starting material because I asked a couple of folks about the starting material let's go back to this.

MR. ALY: Yes.

THE COURT: So you're saying it's done by a lab was it the done by the university or was it done by a separate lab how is what?

MR. ALY: Defendant Alkem retained a lab at University of Wisconsin with professors at the University of Wisconsin and those professors run what they call z laboratory z e been h they are going on be buying that plus 23 because at that point the crystals aren't defined it doesn't really matter these just starting material you need to make sure this is pure.

Are you starting with the right starting material but this was the University of Wisconsin did the following steps in this patents.

Your Honor asked if this is a clinical lab and there was that another, co-defendants have hired is that Organix, that's other name we keep hearing about and Chemic

those are the other labs independently had nothing to do with the university of Wisconsin did their own testing using the same starting material collected to see if it is pure did the crystallization and got the same result which is a mixture of A and B.

THE COURT: Okay. How could the starting material I'm just positing, this is an an open question how would the starting material impact whether you would get A or B okay you're saying you had it tested by a lab to determine it was in fact this substance.

But, could there be variations in that substance that was provided that could yield either A or B or some combination therein and isn't that very important here.

MR. ALY: Very important your Honor and here's what could happen. If you don't know what the starting material is then you actually don't know what you're crystallizing so you might get a crystal of something and it mate have all of the signals why you think form A should be. It may not even be that compound at all.

And an example that happens and we are talking in chemistry here than this was an example that happens here bromine and chlorine these are two atoms on the periodic Table, 2 elements that very very similar to one year and if the starting material is more bromine than chlorine.

Then you don't have the right compound to start

with and then as you go through the proper recipe then you are ending up with something that looks similar to what a form A or a form B but really isn't.

And if you start with impure compound it is an issue and if you start with pure compound you don't know you didn't carryover impurities from the other steps but the way they did it the plaintiffs test if you start with something that you don't know if it's pure or not it could be carrying through these impurities through the process then you would end up with something like look likes a particular form but may not be the right compound if it is right compound it mate be the impurities that are causing it to look in a particular form and this is where impurities basically can come found the results of a particular form A or form B signal.

This isn't just our theory defendants plaintiffs themselves had puts in their internal reports and presentations we are looking at form B it's little weird because form A is the one stable at room temperature so what explains it impurities the problem is probably the explanation and you will see that in their own presentation goes the.

THE COURT: And would doing the process to generate the substance in a certain way following certain steps in a certain order or different steps would it impact also would whether you get form A or form B or some combination.

MR. ALY: No, not if it's above that and you

check what you have right there. The key is right there before you are doing crystallization. What's your starting material before you are doing crystallization if you have this material right here, it doesn't matter how it was made or how it got there.

And in fact that's something that Dr. Buschmann is going to talk about there's different ways to manipulate compounds and solutions and you can there are tricks basically if you have O in a particular position you can put in reagent it will take the O. Off if you have H. Over here and you want to add something to it there's solutions and that's chemistry and some might call will Alkem.

But that's basically what they do make the compounds by adding and subtracting pieces and and subtracting reagents that's what's happening in the first and second steps and they are defined in the patents but the key is the third step when you have and you haven't crystallized anything. This is where the crystallization happens. It has very, very pure material the input crystallization if you trying to get a patents on crystallizing that's the step that matters. Is the crystallization step you got start with right material do the right recipe and end with the right form.

THE COURT: When you buy the substance do you know how it was made?

MR. ALY: When you buy the substance, you don't

always know how it's made. Here for example we can't go back and ask all the people in the labs making the material but because Wisconsin did it in connection with the litigation.

They did have the opportunity to ask all the people how it's made and get additional documentation from anywhere in the chain and they can find out information in but your Honor that's not what matters we don't have to prove that it was made up to that point in the same way and there's not really any science that would show why anything in the earlier steps would really effect if you've got the starting material here.

This is kind of where Mr. Fitzpatrick's analogy works for us which is this flour in the cake. If you're trying to make flour from grain and then sowing and then doing processing you have to do, you don't really know what your starting material is could it could be flour, it could have flour with husks in it.

I don't know what the right terminology is but if you buy flour off the shelf and scientifically test it to say this is an NMR test. It's 99 percent flour then you doing the step properly. So in way we're saying it's a lot better to get it commercially made and done because then you don't have this risk to having carried down impurities or the not knowing what it is you're actually crystallizing so that is the starting point.

THE COURT: Although if you did it yourself you would have full authority and there's no question as to what was contained in the substance by doing it yourself. So you have full authority over verifying exactly what process you used, what was put into it in terms of the contituents and you would have you know a full understanding of what was created and how it was created.

MR. ALY: Yes, your Honor but to be honest that question is to a chemist the same as saying you should have started with the field to make sure why that you used flour at the right step because frankly speaking even the plaintiffs test that the work that he did in making this up.

It didn't start with carbon by itself and hydrogen by itself and then making those bond and then having those form rings and then having those be added into bigger complexes and then hang that two plus two compounds they starting with start material there are rings that already exist with components on them it's not like plaintiffs can say I can show you where those rings were made and how these pieces were attached to.

At the very beginning of even their first step that's chemistry where they take the material put it together and see what it makes. But the key is you got a check it to see that you really got what you made and not just something else that happened to be part of the process.

THE COURT: Okay. Thank you.

MR. ALY: Thank you, your Honor. The University of Wisconsin did all of the tests that were were required to be done on the purity starting material and then they ran through the example 25 procedure and that's what they found at the end of the day was you get a mixture of form A and B.

The next slide 35 I want on show why they didn't follow the recipe and here your Honor was asking Mr. Sitzman for batch 0 is it really the same as example 25 and he conceded it isn't.

Now that's because this his analogy he used 1423 but it really isn't that simple because the material in batch 0 and we'll see that with Dr. Buschmann really wasn't following example 25 even for that third step. The only important step is the third step what they title third step in exam will 24 and Dr. Buschmann didn't use that third step he used something different.

So if I'm saying the crystallization step has to be done correctly I'm saying batch 0 he wasn't done in the crystallization it didn't have to do the precursor up above he didn't have the right starting material and Marita Mueller the other person who did the replication later in 2002 also didn't follow the recipe.

And what I mean by that is there is a step in the example and I'll go back just to show us here in example 33 where we are taking this trimethylchlorine/water reading from

column 18 about Line 72. It's an examination of those two things that u why make and then add it to the solution that is really close to the crystallization you see that after you add those things in example 243.8 grams of hydrochloride crystallized out.

So that's the crystallization component that's very key at the end of the crystallization.

Reading that recipe the University of Wisconsin and Organix put the two together the trimethylchlorine and water together and that's what they dropped and got white powder example 25 shows that they don't report the color the testimony shows it should be white powder and then at Organix they also did it and got white powder.

Interestingly when Marita Mueller did the replication she added the water first and then this other ingredients. What happened is the yellow powder. She called it mustard colored that was the translation the mustard colored powder. This already shows you there's impurities present in what work occurred there's impurities because why it would be yellow.

They haven't provided an explanation the the plaintiffs have not about why anytime else they are make can it it's white when Marita Mueller does it it's yellow this could be one explanation there are several others but you're having either impurities carried through or you're not doing the

recipe in the correct say either way the result we know is going to be mustard yellow.

Marita Mueller asked about that deposition to make sure that her starting material this is again that plus 23 compound on slide 26 the question was presented. If she examined the purity of the 351-1 chemical product which is what we are talking about here at any point in your experiments the answer was no. She didn't check to make sure he had the right ingredients.

Slide 37 says that Mueller when doing the internal work didn't even match up the amounts properly. So so slide 37 the recipe says use 4 points 3 grams of plus three and down here this is the compound that's there we don't know if it's pure or not but the many amount that's use is different 4.55 you're supposed to use a hundred milliliters of hydrobromic acid, she used 11.47, the explanation is using math to scale up things because she wanted to use a little more, didn't want to be so precise on measure but the fact of the matter is she didn't follow the recipe.

Starting with the wrong materials she did the wrong sequence. We explained how the sequence was different the patent says trimethyl chlorine/water do it together. Her procedure says mix first with water and then with the MCS. So it's the two steps rather than doing it in one it's the wrong sequence now I know that Mr. Sitzman said cream and sugar to

your coffee it is only in the following way if you add cream and sugar first and stir it it's lot easier to make sure the sugar is dissolved and you put it in there because you can check that.

If you put them both separately in there you sugar the a bottom cream on top that's what I do every morning if that's what Sitzman is saying not the same thing or it shouldn't be considered the same thing.

It's not unfortunately chemistry that we are talking about here, it's a little bit more complicated than cream and sugar anyway.

That may explain it though because Miss Mueller did these materials differently. Slide 29 the record says mustard colored solid. That's the translation and that's our picture of it because we don't have importantly your Honor we do not have any of the samples that plaintiffs say they tested. The batch 0 doesn't exist anymore. The Mueller doesn't exist anymore as contrasted with the defendants who had the material. I don't think plaintiffs asked for it because had they asked for it in the course of discovery we made the material during litigation we had it available for testing have it available for testing still.

The point of the matter is we don't have sample to see what went wrong we do have our example that plaintiffs could confirm if they wanted to what went right.

This idea about stability your Honor I just want to give an explanation for why stability matters. The form A is like a spring with position A it's coiled in because that's the natural position it wants to stay in somebody can't put force or energy or do something to put it into another position the spring that would be form B position B here.

But if you let go of that or just let it rest back to room temperature, for example, with Tapentadol it's going to go back to form A. That's what their internal report shows and that's what I am trying to show with slide 40. I'm trying to show with slide 41 to answer your Honor's questions about impurities and what could be changing these forms and what you get if you put something in that holds it in place these are impurities like pencils in a spring came to mind that's when you're going to stabilize and see from B when you otherwise wouldn't. So you have to make sure the impurities aren't there.

Now we are getting to slide 42 as we wrap up and that slide is showing the fact of the what I told your Honor about in the beginning they are saying they have material that was prepared according to example 25. European patent which is the same as the '737 example which is the same as example 25.

If you fix the stereo chemistry and they are saying that there was starting material which their internal material says A and then they they are saying as result of that

they got form A but that's what we going to show is this is unclean hands issue which is is if you had form A to start with but you toll the Patent Office something different, clearly they are going to have a different interpretation of what it is that you invented and they are going to say all right you took something over here that was different and you made it into something else. But in reality they had something that was form A and they turned it into form A.

Next slide 43 shows that this wasn't new because because on slide 44 I told your Honor I would stay in the timeline where they did the tests to show Grunenthal what the form was and in 1998 they did it themselves and farmed it out I think FNE is the name of lab. I think I heard where they go this place and they get report of crystal structure in 1998 and they get back form they don't call it form A yet but they get back what I call monoclinic cell parameters. Monoclinic we now know is form A and it provides dimensions for what shape should be is it rectangular or not.

And is that's where that exact number surprisingly are the same ones that they put in the '364 patent event in 2005 as the dimensions for what they are claiming is brand new form A which is for example. A is 7.11 and '364 and in this 98 report it says 7.110. B in the '364 the patent 11.62 B says 11.615. I'm not reading all the numbers but the point is they are the same.

My co-counsel explained the obviousness issue that it's essentially the FDA was asking for in 1987 and slide 46 I explained I I'd showed your Honor that what happened here is that eat was formed out by Grunenthal to two lasts SSCI is one crystallics is another one.

Crystallics they asked also to test it use the usual procedures to test it. And crystallics sent back a report and says we tried 97 experiments we've got two forms thats what we got form A and form B and they are also reporting that form A is thermodynamically stable one meaning that's the one that would be there at room temperature so the question presented is from an obviousness points of view now and these what I'm shifting to putting the test aside from an obviousness points of view if there are two choices A and B and you're doing routine testing is it fair to claim one of those polymorphs and say that's an invention.

It's not part of what counts as an inventive looking at slide 46 I want to make it clear that here the test is not absolute predictability now Mr. Sitzman had a very nice slide with all kinds of options that were there and the analogy that came to my mind if I'm flipping a coin and I get heads or tails, I didn't tell where in the world the coin came from. I didn't tell you the denomination of coin. I didn't tell you what I am going to use the coin for. But I knew I was going to get A and B. That's not inventive.

Another way to look at it using legal tests instead of analogy is what would a person of ordinary skill in the art do given the FDA's instruction to test something for polymorphs. And the new drug Tapentadol at the time what would they do, the person of ordinary skill in the art would do a screen. Maybe they would hire a lab.

Crystallics is one of those labs. They would run their screens and say here's what you get form A and form B. It's no different than taking a blood test and that is not patentable.

Under Mr. Sitzman's view showing that flow chart with the different options and ping pong balls on one side importantly his view is every time I see a polymorph no matter what, I can patent it. Because they would always be true that you would have to test it to figure out what shape it's taking is it a square, is it a rectangle, a rhombus. You have to test to main find that out that doesn't mean its inventive that you've done the same thing that was done for 30, 40, 50 years and you say here I have got a result that's a square because I have a new compound and somebody else does the test and says I got a square too, but they get an invention on that, they get a patent on that?

This is the problem with the timeline that I started with your Honor that what Grunenthal has patented here and what now Depomed is asserting a patent on two polymorphs

that exist they picked one of them and then I think in no else can use even though they did nothing special to get it they don't show anything different that form A does versus B in the body it doesn't make a difference and A is actually the easier one to get because you get it at room temperature as opposed to having to cook it to '130 degrees Farenheit or more. So predictability is not the test obviousness is.

And that's where we're going to conclude by saying that because of the timeline and notwithstanding that Grunenthal did what it did and notwithstanding that Janssen brought these claims and these patents slide 47 is showing what our expert Mr. Hoffman will explain in more detail as the secondary considerations expert but summarizing these numbers in the right hand column.

It's cumulative losses see the lines here were supposed to show how much are we getting on net basis because Nucynta and Nucynta IR ER and immediate release and the answer is negative numbers every year negative numbers and in 2014 finally they have accumulated the losses now it's over $400 million in losses that they have e an accumulated.

So, when Depomed says hey we're willing to pay money for that this is not a situation where Grunenthal or Janssen are saying no please don't we're e making tons of money on this they are saying we've lost $400 million and if you're going to give us money on that sounds like a great deal it

doesn't mean that there's anything inventive here about it.

It just means these are the numbers or the financial situation is the parties happen to find them also and that's what the secondary considerations will say is that none of these numbers even if they were positive sales weren't because of the polymorph certainly weren't because of the new method because the method is about one percent of the usage they were because if anything the Tramadol development that happened in 70s.

And for that reason we believe that all three patents should be found invalid because they it didn't really add anything to the prior art. Thank you very much your Honor.

THE COURT: Thank you so much. All right. Much appreciated. Thank you that was quite helpful, everyone's opening statement to the Court. I do appreciate them. And again I have listened very carefully so I think it sets the stage for us moving forward quite nicely.

At this point do we intend to introduce our next our first witness, rather I know it's 4:30. It's basically how you folks would like to handle this at this point.

MR. SITZMAN: I think if it's okay with the court we would like to at least call our first witness.

THE COURT: That would fine.

MR. SITZMAN: Who is fairly short. But that

does mean that tomorrow could be a long day. Dr. Buschmann and Dr. Gruss are both here from Germany and they will have to testify tomorrow.

THE COURT: Do you anticipate they will both be done tomorrow?

MR. SITZMAN: That's what my hope is and I think that if the Court will indulge us and we do get through that then I think we can continue to accommodate the defendants on Friday.

THE COURT: All right. And again who do we have schedule for Friday.

MR. SITZMAN: Friday we have Dr. Haussler from Janssen in the morning.

MR. CAPUANO Dr. Weinberger for Actavis.

MR. SCHULER: And then Dr. Mogil. On behalf of the entire defense group, we will call Dr. Mogil.

THE COURT: Do you think you will be done with all three of those on Friday?

MR. SCHULER: Counsel indicated that Dr. Haussler is relatively short and I am fairly confident we can get all of those in.

THE COURT: Then let's take a break then we will start our first witness here today. It sounds like you may be able to conclude that today.

MR. SITZMAN: Yes.

THE COURT: That sounds fine. Thank you.

(Whereupon a short recess was taken.)

THE COURT: Let's have the plaintiff call their first witness.

MR. SITZMAN: Thank you, your Honor. Jack Anders.

J A C K L. A N D E R S, sworn and testifies as follows:

MR. SITZMAN: Your Honor, we've got witness binders for the Court.

DIRECT EXAMINATION BY MR. SITZMAN:

THE COURT: The witness has been sworn.

Q. And where do you work?

A. I currently work at Depomed.

Q. And in what business is Depomed engaged?

A. So we are a pharmaceutical company focused on pain and treatment of the central nervous system.

Q. And how big a company is Depomed?

A. So we are approximately 500 employees. From a market cap perspective at about 900 hundred million to a billion.

Q. Okay. And how long have you worked at Depomed?

A. I've worked at Depomed approximately ten years.

Q. And what is your current position at Depomed?

A. Vice-president of finance.

Q. And could you describe for the court your, generally describe your duties as vice-president of finance?

A. As part of my duties I am in charge of the FNPA finance which is financing planning and analysis. So budgeting, tracking performance versus budget, doing ad hoc financial analyses including financial modeling, product acquisitions, company acquisitions.

Another part of my team is focused on commercial finance. So revenue recognition, you know, invoicing, collection with regard to our product sales. As well as part of my job includes drafting pieces of ICC reports and reviewing some of those respective filings.

Q. Okay. And speaking of your products and your product portfolio, can you generally describe or specifically describe for the Court what the Depomed current product portfolio is?

A. Sure. We currently have six products, two of which are in question here. So, Nucynta and Nucynta ER. Our four products Gralise, for post tympanic neuralgia?

THE COURT: What was it?

THE WITNESS: Gralise, for post tympanic --

THE COURT: Could you spell it?

THE WITNESS: G-r-a-l-i-s-e.

THE COURT: That is for.

THE WITNESS: It's PTN, which is post tempanic neuropathy. It's a nerve pain.

THE COURT: Thank you.

Q. I don't know if you've recited all of the products?

A. No. So we also have Cambia, C-a-m-b-i-a, which is indicated for acute migraines. And we also have Zipsor, which is indicated for mild to moderate acute pain. And lastly we have Losonda, which is indicated for pain associated with late stage cancer.

Q. Are these on the demonstrative up here which looks like it's got a picture of Depomed, are those the labels or all or the actual names of all the products that are currently in the portfolio?

A. That is correct.

Q. Okay.

MR. PATEL: Your Honor, I don't know how many demonstratives they have, but we did not receive any copies of the demonstratives.

THE COURT: Do you want to just take a quick look? I don't know if we will cover all of them today.

MR. PATEL: This is the only demonstrative.

MR. SITZMAN: This is the only one.

THE COURT: Okay.

MR. SITZMAN: Are there any objections?

MR. PATEL: No objection.

THE COURT: No objection. Good.

MR. SITZMAN: Sorry about that.

Q. Which of these products generates the most revenue for Depomed?

A. It's the Nucynta franchise which is about 60 percent of our total revenues.
Q. And that's Nucynta and Nucynta ER?
A. Correct.
Q. Now what is Tapentadol?
A. Tapentadol is the active pharmaceutical ingredient in both Nucynta and Nucynta ER.
Q. Okay. And the ER on Nucynta ER what does that stand for?
A. Extended release.
Q. And the other one that doesn't say anything is the immediate release?
A. Correct.
Q. Now, did Depomed develop the Nucynta franchise internally?
A. We did not.
Q. Did Depomed purchase the Nucynta franchise from somebody?
A. Yes, we did.
Q. And who was that?
A. We purchased the rights to the Nucynta franchise from Janssen pharmaceutical.
Q. And when was that?
A. We announced the acquisition in January of 2015 but we completed the acquisition in April of 2015.

Q. And were you involved in that acquisition process?
A. Yes, I was.
Q. And can you tell us just a little bit about your involvement or role in that acquisition?
A. Sure. My team did the financial modeling with respect to the acquisition. My team was also involved in, you know, finance, due diligence, looking at the data room, looking at their, you know, internal P & Ls,some of their contracts for certain financial obligations.
Q. When did you first become involved in the efforts to acquire the Nucynta franchise?
A. I believe it was approximately December 13th, I'm sorry, December 2013.
Q. And can you recall how you first became involved in that process?
A. Our senior vice-president of business develop Fad Vargas (ph) approached individuals with, you know, in the team at Depomed of potentially acquiring Nucynta from Janssen.
Q. And did Depomed make a bid to Janssen for the acquisition of the Nucynta franchise?
A. We did eventually make a bid. At the time Janssen was actually looking for a co-promote partner and not actually a company to acquire the products. But, we actually wanted the products for ourselves. We did not want to go through the co-promotion route. And if you'd like me to explain

co-promotion --

THE COURT: Yes, go ahead.

THE WITNESS: So, co-promotion would be that Janssen would retain the license and the rights to the product. We at Depomed having a sales force, we would promote the product on their behalf to physicians and detail the product and we would get a cut of the profits.

And so that was, you know, we knew Janssen was looking for a co-promote partner. We actually wanted to acquire the products for ourselves because we felt that we could do a better job with the products.

Q. Okay. And at that time -- well, strike that.

Why was Depomed interested in the Nucynta franchise?

A. We really liked the product itself. And so that was obviously part of the interest. It was a, you know, a novel compound. It had certain characteristics that we liked. And also we are, you know, Depomed is in the pain CNS business. We had, we thought there would be certain synergies, you know, with Depomed acquiring the product which included our expertise in pain and our actual you know sales force that has been focused on pain and CNS.

So, you know, we were at that time our sales force was calling on, calling on and visiting physicians who also prescribe Nucynta and Nucynta ER.

Q. At the time that Janssen was looking for that

co-promote, did Depomed make a bid for the acquisition of the Nucynta franchise?

A. So we did put in an unsolicited bid to acquire the franchise.

Q. And how much was that?

A. The first number that I believe we sent over was approximately 400 to $500 million.

Q. And you said million?

A. Correct.

Q. At your deposition did you say something different?

A. I did. I made a mistake. I said 400 to 500,000. The correct number was 400 to 500 million. And you know for a product that was selling 150 to 160 million annually at the time 400 to 500,000 doesn't make any sense. So I did, I misspoke during the deposition which we hopefully corrected with the errata that we submitted.

Q. At the time of the bid, the unsolicited bid, did you have access to any confidential information belonging to Janssen?

A. Not that I'm aware of.

Q. Other than the Nucynta acquisition had you already been involved in other bids by Depomed to acquire other drugs?

A. Yes.

Q. How did Janssen respond to Depomed's unsolicited bid?

A. They eventually decided to go through a formal process

to find additional bidders to sell the rights to the entire franchise. So they shifted it from the co-promote model to an actual bidding process on the sale of the rights to those products?

Q. And I assume Depomed then participated in that bidding process.

A. Yes, we did.

Q. Okay. And do you know how many other companies participated in that bidding process?

A. I don't know the totality of other companies but Janssen did notify us that there were at least four other bidders.

Q. And at that time, at that point in time, did you get access to confidential information belonging to Janssen?

A. Eventually we had had access to the diligence room that they set up.

Q. And you had meetings with Janssen set?

A. Yes, we had, we did have a face-to-face meeting with them in September of 2014, as well as phone calls.

Q. Okay. Let's look at one of those. Can I have PTX 829?

THE COURT: Just before we go through the exhibits, is there any issue with these exhibits? They have seen these exhibits? And you have exchanged the list and these are the list?

MR. SITZMAN: Correct, these were the list.
MR. PATEL: Correct.
THE COURT: No issues, correct?
MR. SITZMAN: Correct.
MR. PATEL: Correct.
THE COURT: Good.

Q. Do you recognize -- Mr. Anders, do you recognize 829?

A. Yes.

Q. What is this?

A. So this is the presentation that Janssen gave to us in person. So we went out to New Jersey to visit them with regard to acquiring Nucynta. We brought a large team out there. They had a large team out there to present the Nucynta products. And so they gave us this presentation live in person and then they eventually gave us a soft copy.

Q. They actually then gave you a soft copy of the slides that we are seeing here?

A. Yes.

Q. Let me just look at a couple of pages here. If we can pull up page Bates stamped Jan Nucynta 1634430. So, it's 4430 in the bottom right corner.

A. Okay.

Q. Executive summary. And the second bullet point is Nucynta is ideally positioned with a broad, robust molecule portfolio.

Do you see that?

A. Yes.

Q. Under that bullet, first sub bullet reads both immediate and extended release products.

Do you see that?

A. Yes.

Q. Was the existence of both IR and ER products and versions of Nucynta a factor that Depomed considered as part of the due diligence process?

A. Yes. We were aware that Nucynta IR competes in a short acting opioid market. And we were, you know, and Nucynta ER was competing in a long acting opioid market. And so you know the presence of both of these was a factor that played into our decision.

Q. Okay. And then the second sub bullet point, sorry, maybe all the way down at the end it says composition of matter patent through 2022.

Do you see that?

A. Yes.

Q. And did you understand that, aside from this composition of matter patent, that there were other patents as well?

A. Yes. I mean it is later in this presentation that there were patents that go out to 2025 and 2028.

Q. Was the existence of these patents and the patent

protection for Nucynta something that Depomed considered an important part of the bidding process?

A. Yes.

Q. And why is that?

A. So as a company we were prepared to make a significant investment into acquiring this franchise and you know including a very large acquisition fee. We needed to really make sure that there were lengthy patents in order for us to essentially have the future revenue stream to you know essentially make back the investment that we would be putting forth to acquire the products, as well as any interest that we would incur in order to make the actual upfront payment. And the patents were a key piece of those future revenues.

Q. Now, under the third bullet point there it says that it is the only CII or CIII opioid with a dual MOA that works through two pain pathways.

Do you see that?

A. Yes.

Q. Do you have an understanding of what that means or what that refers to?

A. So, the dual MOA being the dual mechanism of action was something that we were aware of. We understood that as it says there it works through two pain pathways. The first pain pathway is typical with an opioid. And I'm not a scientist but as we understood it from a deal perspective, you know, the

first, the first pain pathway being the MU opioid receptor agonist, something you know opioids typically work on the opioid receptors. We thought you know that's pretty common with other opioids.

What was different about Nucynta is that it worked on you know through a second pathway which you know it worked as neuro epinephrine reuptake inhibitor. But which was more, as our internal medical team focused on, was more specific towards treating neuropathic pain.

So, it had differentiating features comparative to some of its competitors on the market. And so we thought that this was a very, very novel distinction in order for us to take the product and really think about you know as we tell the story of Nucynta and try to grow the franchise, that this is a piece of that story.

Q. Let's look at just a few more pages.

Can I have page Number 4445 in the bottom right. The title of this slide is Tapentadol has better G.I. tolerability than Oxycodone in all studies.

Do you see that?

A. Yes.

Q. Was the tolerability of Tapentadol something that Depomed considered as part of the due diligence process?

A. Yes, it was.

Q. And was that an important consideration as part of the

bidding process for Depomed?

A. It was an important consideration. Opioids do have a lot of side effects. We felt that having lower side effects than some of its competitors was part of the differentiation of the product. Particularly that in G.I. disorders, opioids, you know, do cause a lot of constipation.

I mean there are drugs out there for OIC, opioid induced constipation. And so we thought that less side effects you know made more, added to the compelling argument on why a physician should be prescribing Nucynta versus some of its competitors and so having less side effects, having essentially a very similar pain profile in terms of efficacy was an advantage for the product relative to some of its competitors.

Q. All right. Let's look a little bit further ahead. Can I have Page 4449?

The title of this slide says Tapentadol has lower rates of abuse versus category.

Do you see that?

A. Yes.

Q. Was the abuse rate of Tapentadol something that Depomed considered during the due diligence process of the Nucynta acquisition?

A. Yes, it was.

Q. And why was the abuse rate of Tapentadol an important consideration?

A. So, we were aware that you know in this category opioids have high rates of abuse, addiction and diversion as well. You know we felt that given the low abuse rates, it is part of the whole you know differentiation story in terms of mechanism of action, lower side effects, lower abuse potential.

So, it really just makes this, you know, this compound that more attractive that it was, it had differentiating features that would allow it to compete in a very competitive market.

Q. And I apologize but I'm going to make you go back to Page 4434. And the title of this slide is Pain market is large, fragmented and evolving.

Do you see that?

A. Yes.

Q. And do you remember this slide from the presentation?

A. Yes, yes.

Q. Where does, in this slide, where does the Nucynta IR product fall?

A. So the Nucynta IR product falls under the middle one Class II SAO category.

Q. The third one from the left, CII SAO?

A. Yes, CII being Class 2.

Q. SAO?

A. Short acting opioid.

Q. The ER product falls where?

A. The one to the right of it CII LAO.
Q. And the CII refers to the controlled II substance?
A. Yep.
Q. And am I reading that correctly in terms of what's being said here, that all of these are almost a hundred percent genericized except for the CII LAO market?
A. Correct. It says the CII LAO market is 66 percent generic.
Q. Is that consistent with what you believe Depomed believed the market looked like at the time of its acquisition or the bid?
A. Yes, it's consistent.
Q. Let me have you look at 4470. And this is entitled Nucynta commercial model has evolved to a specialty model.
Do you see that?
A. Yes.
Q. I just want to ask you a little bit about that fourth area on the bottom there. It says business model. Can you tell me what's being represented there or explained?
A. So, this is the, as Janssen explained to us, the quantity of reps that they had promoting Nucynta IR and ER overtime and how that changed from 2009 to 2014.
Q. If I'm reading that correctly, it looks like that at one point in time they had in excess of a thousand reps and then they went to 89?

A. That's correct.

Q. And did they have any explanation as to why they did that?

A. I don't know specifically their reasons behind that. They did, you know, they did decide to go to this dedicated specialty rep where they had a contract sales organization. So they went away from actually having their own Janssen employed reps to an outsource model. And those, so these were contract sales reps when they switched over to the dedicated specialty 89 reps.

Q. Did that effect Depomed's decision to move forward or effect in any way the bid that Depomed ultimately made for the franchise?

A. It did. We saw this as an opportunity. You know we felt that they were not resourcing this and giving it the attention that it probably needed.

And so we thought that this would be a product with our existing sales force structure that we could take the message of Nucynta and characteristics of Nucynta and really continue to educate docs and target more physicians and really drive growth.

So we saw this as really interesting that they really slimmed the sales force down in 2013 and 2014. And so it really reinforced our ability that we could really grow this product from where it was in 2013 and 2014.

Q. Let me ask you about one more slide in this here, it's Page 4471. It's just the next page up.

Do you remember this part of the presentation?

A. Yes.

Q. And if I'm reading this correctly it looks like there's 56 percent growth in the Nucynta sales?

A. Sure. It's 56 CAGR growth which is the cumulative annual growth rate. So it's increasing 56 percent each year starting from 2009.

Q. It looks like there's 188 million?

A. 188 million in net sales.

Q. In net sales.

Were you here during Alkem's opening statement where Mr. Aly showed some information, some financial information from Janssen?

A. Yes, I was.

Q. And do you recall him showing that it was a $400 million loss to Janssen?

A. Yes.

Q. Did you understand that that was, at the time that Depomed was looking at this product, that that was a $400 million loss to Janssen?

A. So, I don't know specifically. I didn't add that to get to the 400. But, there is information in this management presentation that does show their internal P & L where they

were at losses in the first three to four years.

It's typical in a commercial launch. You don't, as you see here, you don't have the revenues to generate to offset of the expenses. And typically with some of our products we haven't been profitable on launch and it took awhile, it took a few years in order to get profitable.

But, we also you know, I can't really speak to the expense structure that Janssen had in place and how they allocated those expenses. The way we viewed this product, and you know we obviously knew it was at a loss in those first few years, and you know we take that with a grain of salt.

But, in our hands it's, you know, it's a different story. Depomed has a different cost structure. This is a product that at that time was doing $188 million in 2013. It made a lot of financial sense for us to take on this product.

Q. Let's talk about the actual acquisition.

Can I have Exhibit 1563? And let me know when you're there.

A. Got it.

Q. Do you recognize 1563?

A. Yes, this is our annual report on form 10K for the year ended December 31, 2004 that we filed with the SEC.

Q. You said 2004?

A. I'm sorry, 2014.

Q. It's okay. Sometimes numbers don't come out right.

Were you involved in the preparation of this document?

A. Yes, I do draft certain portions of the document and I did review the entire document.

Q. Okay. Let's look briefly at page DM.0020.

How much did Depomed ultimately bid for the Nucynta franchise?

A. So the final and winning bid was at 1.05 billion with a B.

Q. With a B. Do you know what the other bids were for Nucynta?

A. I do not know the other bids.

Q. Where did Depomed get the $1.05 billion that it needed for the Nucynta acquisition?

A. We didn't have it and we ended up borrowing 920 million in order to do the acquisition. And we funded the remaining 130 million with our existing cash.

Q. If you look forward in the document I think it's Page 118, there's a note 8 in the disclosure. It's labeled debt. Do you see that?

A. Yes.

Q. And what's the subject matter there that's being reported?

A. So this is the, so we took data out in two large tranches. This is the first tranches debt which is convertible debt. So it converts into our actual shares of Depomed common

stock. But, with this we borrowed 345 million in convertible debt.

Q. Let's jump ahead. Let's look at Exhibit 1568.

Do you see that document?

A. Yes.

Q. Can you tell us what that is?

A. So this is our quarterly report on form 10Q that we filed with the SEC and it relates to the period ending September 30, 2015.

Q. And again this is a document that you helped to prepare and file?

A. Yes.

Q. Okay. Let's pull up Page 406, DM 00406. And there I'd like to look at note nine that also says debt.

A. Okay.

Q. And what's the subject matter there of this particular debt?

A. So this is the second tranche that I referred to. So this is 575 million in senior notes that is not convertible.

Q. Is Depomed paying interest on this loan?

A. Yes, we are.

Q. And what is the interest rate that Depomed's paying?

A. It's pretty high. It's a floating interest rate. But as we sit here today it's 10.75 percent interest.

Q. Is Depomed also required to make principle payments on

that loan?

A. Yes. So starting on the third anniversary we start to make annual principle payments or we are required to make principle annual payments.

Q. And I think there may be a chart on the following page, Page 407.

Does that set forth some of the principle payment obligations?

A. Correct.

Q. Is this loan secured or unsecured?

A. It's secured by all of our assets.

Q. All of Depomed's assets?

A. Correct.

Q. What happens if Depomed can't make its loan payments?

A. There's a lot of possibilities that could happen. The holders of the debt could seize the assets. They could make us liquidate the respective assets. So it could be us having to sell some of our existing products. And so, you know they you know they would have control of our assets and could dictate what we do with them.

Q. Let me have you turn to Page 437 in the same document. There's a section called risk factors?

A. I'm there.

Q. You're there. Okay.

Did you help prepare portions of this disclosure here?

A. This is an area that I reviewed.
Q. And at the top of Page 438 it discusses generic manufacturers and litigation?
A. Yes.
Q. Okay. And what's the risk that's being disclosed there?
A. So, the risk is essentially that, as I mentioned, if generic manufacturers use litigation in regulatory means to obtain approval for generic versions of our products, our business will suffer.
Q. And based on your analysis and work, would Depomed be able to make its payments on the $920 million in loans if generic versions of Nucynta were to enter the market this year?
MR. PATEL: Objection, your Honor. I just want to object to this line of questioning on relevance grounds.
THE COURT: Well, you know what, it is a bench trial and I am obviously dealing with all of the issues here since we do not have a jury. So I'm going to let counsel continue.
And obviously I'm going to weigh it myself and determine how much to value it. All right. Thank you.
MR. SITZMAN: Thank you, your Honor.
Q. You can go ahead.
A. As I mentioned, Nucynta, the Nucynta franchise represents 60 percent of our revenues. We you know internally

we always look at and we run our own case studies and analyses in terms of what happens when a generic entrant comes onto the market.

What we have seen is you know within a year, prescriptions of the brand product typically you know drop 75 to 95 percent. So this being a product that's 60 percent of our revenues, you know, our expectations would be that we would lose a lot of prescription demand and lose a lot of associated revenues. We just, we wouldn't have the cash flows to make those respective debt principle payments.

Q. The ones that are secured by all the assets?

A. Correct. And as well as the convertible debt, which is it is due in seven years.

Q. Okay. Now since Depomed acquired the Nucynta franchise, have any companies expressed an interest in obtaining Depomed or Depomed's rights to Nucynta?

A. So, we did have an unsolicited proposal from Horizon Pharma to acquire the company.

Q. And approximately when did that come relative to the Nucynta transaction?

A. So we closed the Nucynta acquisition in April of 2015. Their CEO actually reached out to our CEO prior to then. Our CEO said wait, we're in the middle of closing the transaction. You know, talk to us afterwards.

They immediately made an offer in May of 2015 and we

rejected that offer. We eventually, you know, we launched the product with our own you know revamped commercial team in June of 2015. And then I believe it's in July of 2015 they made the acquisition attempt public and it turned into a hostile bid.

Q. Horizon, did you subsequently learn that Horizon was one of the bidders for the Nucynta franchise from Janssen?

A. Yes, we were aware they were one of the bidders.

Q. And obviously they were not the successful bidder?

A. Correct.

Q. And now they were making a hostile takeover for Depomed?

A. Yes.

Q. Ultimately did those efforts succeed?

A. No, they withdrew their bid in November of 2015.

Q. All right. Let's just turn briefly to Nucynta's performance at Depomed.

Let me have you look at exhibit PTX 1559.

A. Okay.

Q. And do you recognize this document?

A. Yes, this is our third quarter 2015 earnings release.

Q. Okay. It's dated November 9, 2015?

A. Yes.

Q. Were you involved in putting together the information that's contained in this press release?

A. Yes, I helped draft this. My team provides all the

numbers in this document.

Q. In the third quarter of 2015, how did Depomed's net sales for the Nucynta franchise products compare to those realized by Janssen?

A. So, if you look down on that second bullet, so Nucynta's net sales for the third quarter of 2015 were 65 million. So the corresponding period a year ago Janssen reported in the low 40 million range.

So this is an increase of about 50 percent over what Janssen recorded as net sales for the Nucynta franchise in the same quarter in 2014.

Q. And I just want to make sure I got the number right, 50 percent, five zero?

A. Over 50.

Q. Let me have you look at Exhibit 1566 and ask if you have seen this document before?

A. Yes. This is our, the investor presentation that our CEO and CFO typically give to investors and analysts. And this was presented in January of 2016.

Q. Were you involved in putting together the information that's contained in this presentation?

A. Yes, I do review it and I do provide the numbers within this document.

Q. Let's look at page DN 356 titled Promotion progress: Accelerating demand RX growth of 20.5 percent over prior year.

Do you see that?

A. Yes.

Q. How well has Nucynta ER performed in terms of market share since Depomed acquired the Nucynta franchise?

A. So the market, since we acquired the franchise market shares are up about 19 percent. What this graph shows is really the, you know, the year over year prescription growth.

I think what's important to point out is you know Nucynta ER was growing when we acquired it. So if you look at the May 2015 time frame on the left, it was growing in the single digits.

In June of 2015 is what we called the Depomed launch. So that's what -- the Depomed launch is us going out hiring additional sales reps, training them on the product, training our existing sales force on the product. We came out with a new campaign for the franchise and we started you know promoting, promoting to physicians ourselves as Depomed. And so that occurred in June 2015.

What you do see is it took a little bit of time but you do start to see we started to accelerate the prescription growth. So it went from single digit year over year growth prior to our launch to, you know, approximately 20 percent growth over the prior year in November, December.

Q. Okay. And this is prescription growth, right? I misspoke, I said market share or something like that.

A. Yes.
Q. But let's look at market share.
A. Sure.
Q. I think that may be on slide 358.
A. Okay.
Q. Did I get this one right now, market share?
A. Yeah.
Q. So how has the Nucynta ER performed in terms of market share?
A. We've grown market share, we've grown market share by 19 percent in approximately seven months.
Q. Did Depomed lower the price of Nucynta ER to make up this gain in market size?
A. We did not lower the price. We did increase the price on acquisition in April of 2015.
Q. So you've made this growth despite the fact that the price has increased?
A. Correct.
Q. Actually, let's just turn ahead, or back, sorry about that, Page 348.
Does Depomed expect the revenue from Nucynta to grow even more?
A. Yes, we do.
Q. And it looks like on the front line it says billion dollar blockbuster opportunity?

A. Yes.

Q. Okay. Does the length of time that Nucynta enjoys patent protection bear upon this expectation?

A. It does. You know it will take sometime to get to a billion dollars in net sales. But, with the added patent, it's something that our management team thinks we can get to.

MR. SCHULER: Your Honor, I just want to make sure that if the plaintiffs go any further, that Roxane's position is they are awfully close to waiving the attorney/client privilege.

MR. SITZMAN: I don't see that but that was my last question.

THE COURT: I don't see it either at this point.

MR. SITZMAN: Thank you. I have no further questions at this time.

THE COURT: That makes that easy. All right. Who would like to do cross?

MR. PATEL: I will be doing the cross.

THE COURT: Will you be doing the entirety of the cross or is everyone going to do part?

MR. PATEL: We will see. I will probably be handling most of it but other defendants may have other questions.

THE COURT: Go right ahead.

MR. PATEL: I think we have some binders too.

THE COURT: Hand them up.

CROSS EXAMINATION BY MR. PATEL:

Q. Good evening, Mr. Anders. I guess it's late enough to be evening.

A. Good evening.

Q. Mr. Anders, earlier you were discussing the sales of Nucynta with Mr. Sitzman. Do you recall that?

A. Yes.

Q. And the sales in particular at Depomed?

A. Yes.

Q. Now one of the things that Mr. Sitzman mentioned is that Depomed instituted a price increase, correct?

A. Correct.

Q. And would that price increase -- that price increase would also increase the revenue that Depomed was obtaining for Nucynta, right?

A. That's correct. We do retain some of that price increase. We do have to, there's certain governmental programs where we don't get any benefit from the price increase and certain managed care contracts out there where we don't get the benefit. But, largely we do in totality we do get part of the price increase.

Q. Okay. And let's talk about the price increases that Depomed instituted.

Is it correct that Depomed immediately increased the

price of Nucynta, upon acquisition, by 44 percent?

A. That is correct.

Q. And was that at the time of acquisition in April 2015 or the time of this joint launch in June 2015?

A. So, it was immediately when we acquired the product.

Q. So April 2015?

A. That's correct.

Q. Okay. And isn't it true -- and Nucynta comes in a variety of doses, right?

A. Yes.

Q. And Mr. Sitzman, and I believe you testified about the immediate release dose and the extended release dose, extended release formulation, right?

A. Correct.

Q. Is it correct that Depomed increased the price of one of the ER doses shortly after acquisition as well?

A. That's correct. So we did have the same price for the 200-milligram and the 250-milligram Nucynta ER products. So, as the management team we did, they had the same price and in June of 2015 we did increase the price of the Nucynta 250-milligram by 25 percent to make it a little more promotional to the actual milligrams.

Q. So, that was increased by 25 percent.

And in December 2015 is it correct that Depomed added another nine percent increase over the entire Nucynta

franchise?

A. That's correct.

Q. So, if we're just doing the math, that's about a 53 percent, over 50 percent increase on the Nucynta franchise except for the 250-milligram dose?

A. Yes.

Q. And that's in the less than eight months that Depomed was marketing the product?

A. That's correct.

Q. And if you're looking at the 250 milligram dose, we're talking about almost an 80 percent increase in price?

A. I think that's a fair assessment.

Q. And so when you were discussing with Mr. Sitzman earlier about the revenue growth that Depomed experienced, you testified that you experienced about a 50 percent growth in the third quarter compared to what Janssen was making, right?

A. That's correct.

Q. You would agree that these price increases that we just talked about contributed to those increased sales numbers, right?

A. They did have an effect. But, I do think I was referring to Q3 net sales. And I think what you just mentioned that you were referring to is the December 2015 price increase. So, that was done after Q3 of 2015 and those net sales numbers.

So, you know, the characterization that we increased

the price by over 50 percent as it relates to the testimony then I mentioned in terms of the over 50 percent net sales increases is incorrect. So it does include the initial 44 percent price increase but it does not include that.

Q. The subsequent nine percent?

A. Yes.

Q. So we're still at 44 percent increase still. You would agree it had a significant impact on the increased --

A. It did. To put it in perspective, we launched the product in June and it takes time to, you know, get physicians to write the product. So our Q3 you know net sales isn't -- you know, we did increase Nucynta ER prescriptions and we started to accelerate the growth. But, we started to really see the effects more so in Q4 versus Q3.

Q. Okay. And we'll get to those sales numbers. But, sticking with price increases, isn't it true that there are more price increases planned for the future?

A. So, in our financial models consistent with you know the industry, we do have modeled in our long term forecast once a year price increases in the high single digits.

Q. About nine percent every year?

A. Yes.

Q. It's year over year?

A. Every year one.

Q. And isn't it true that as Depomed gets closer to

generic competition, those price increases will be even more significant?

A. In our model, that's correct.

Q. Approximately 20 to 30 percent, right?

A. But you know there's a lot of things that could happen between now and then that would make us do things differently.

Q. Exactly. Let me ask you about, you said that you've done things differently. One of the things is increase marketing, right?

A. Yes.

Q. And isn't it correct that Depomed increased its sales force by over three times what was at Janssen?

A. So yeah, if you look at the specialty sales force that was put up on the screen earlier, that was, you know, approximately 89 sales reps were currently out there with 275 sales reps promoting the product.

Q. The increased sales and marketing certainly had an impact on the increased revenue that Depomed experienced, right?

A. You need to tell the story. So, really you know we felt there was an opportunity to increase you know the promotional efforts, including sales reps. But, you know that was a portion of it. But, you know, the key is getting the message out and for us was getting the message of dual mechanism of action, the lower side effects and I think it's

telling physicians about the product. And increased sales reps kind of helps us educate physicians about the product in that manner.

Q. Earlier you were talking about some of the benefits that you believed that Nucynta has. You called them novel. You said that there was less side effects.

Sir, you're not a medical expert, right?

A. That's correct.

Q. Those are just statements that you saw in the Janssen presentation that you were testifying about?

A. So they were in the management presentation that Janssen prepared for us. You know I've had conversations with our scientific folks that corroborate what was in those respective presentations. And so --

Q. But you're not an expert?

A. I'm not an expert, absolutely not.

Q. Right. Correct?

A. Correct.

Q. Now, isn't it true that Depomed's CEO attributed those increased sales to the efforts of its sales force?

A. I don't know that. Can you --

Q. Sure. If we can turn to, I believe it was the earnings, third quarter earnings report, exhibit PTX 1559. If you look at -- and Mr. Sitzman was asking you about this. And the revenue growth and the last, there's a quote from Jim

Schoeneck the president and CEO. And right at the end of the sentence there he says the increased revenue is reflecting the outstanding work of our sales force across the entire product line.

Does that refresh your recollection?

A. Yeah, but, that doesn't specifically say that it's because we increased the sales force.

Q. Let's talk about what else happened at Depomed.

There were no additional indications that came out once Depomed acquired the product, right?

A. You're correct.

Q. There were no new patents that came out after Depomed acquired the patent, right?

A. Correct.

Q. And you testified that it was Depomed's promotional efforts that led to the increased sales, right?

A. Yes. I could be specific in this sense. It's us, it's our sales reps getting the message out of the benefits of the product. And so part of our campaign, part of the education of our sales reps was for them to really hone in on the dual mechanism of action.

And so it's part of the educational efforts that our sales reps went out --

Q. Isn't it that Janssen was also marketing for dual mechanism action? You just increased the size of your sales

force, right.

A. I don't specifically know specifically what Janssen, what their marketing campaign was.

Q. It was something that attracted you to this product, right?

A. Not their marketing campaign.

Q. Not the marketing campaign. But, the dual mechanism of action is something that attracted you to this product, right? That was something that Janssen had told Depomed about and was marketing it through its sales force as well?

A. I can't speak to how effective they were in getting that message across. But, we made that a priority point of our marketing materials.

Q. You say it was better in your hands, meaning you were able to execute better on promotion and marketing compared to Janssen.

Do you agree?

A. Can you repeat that question again?

Q. That you said that the product was better in your hands, which means that you believed that Depomed was better at promoting and marketing the product?

A. Yeah. We felt we could do a better job.

Q. Again, there were no new indications, no new patents. It's just through promotion and marketing?

A. If you look at our new campaign, so we came out with

the new campaign and new promotional materials to educate docs. It was really heavy on the dual mechanism of action that, you know, this addresses two types of pain, nociceptive pain and neuropathic pain. And there's one product that can address it. And so we emphasized that that was a key driver.

And I can't speak to exactly how Janssen's sales reps were promoting the product, but, that was our strategy and it seems to have grown prescriptions.

Q. And that's a sales strategy, right?

A. It's a sales strategy.

Q. Let's talk about the forecast. You talked about how Depomed has high hopes for the Nucynta franchise, right?

A. That's correct.

Q. And now you said that you participated in the due diligence process.

Is that right?

A. Yes.

Q. And during that due diligence process you knew that Janssen had a cumulative loss, right?

A. I did receive, you know, their internal P & Ls. But, as I mentioned before, it's typical you know in the commercial launch you typically lose money in your first few years. It's something that we have experienced with our products. It's something that we've experienced when we've acquired products.

Q. I heard you about the losing money during the first few

years. But, isn't it true that Janssen had a $400 million cumulative loss?

A. I don't have the numbers in front of me and it may have been.

Q. You saw the management presentation, right?

A. Yes. It could have added to 400, I just --

Q. Okay. Now, in terms of forecasts, did you ask during the due diligence process whether Janssen met its forecasts?

A. No.

Q. So you weren't aware that Janssen fell well short of its expectations or forecasts?

A. We were not aware of that.

Q. And isn't it true Depomed is a much smaller company than Janssen?

A. That's correct.

Q. You would agree that Janssen is a sophisticated pain company?

A. I don't know a lot about Janssen and whether they're a sophisticated --

Q. You were deposed a few weeks ago and I can read your testimony if you want.

Do you recall testifying that you believe Janssen was a top five pain company?

A. Sure. But, this is different from a sophisticated pain company.

Q. And Janssen is one of the largest pharma companies in the world?

A. Right. I said it's different from sophisticated.

Q. Now, Depomed's forecast, they are based on assumptions, right? There's plenty of assumptions that are in those forecasts?

A. Yes.

Q. And in fact isn't it true that any investor presentation talking about future sales that Depomed may hope happens, has a warning in there that says no assurance that anticipated results will be achieved?

A. That's correct.

Q. And that's because there is a significant risk that those forecasts may never be met?

A. I disagree that there's a significant risk, but, there is a risk. And that's why we put that disclaimer in.

Q. There's a whole laundry list of risks that you included in your SEC statements?

A. That's correct.

Q. It's really just a hope and expectation. It may or may not happen?

A. It's our current forecast but you're correct, it may not happen.

Q. And there's lots of unknowns. For example, in the pharmaceutical space there could be a new product that could

make Nucynta obsolete, right?

A. It's possible.

Q. Okay. Let's talk about the sales of Nucynta currently at Depomed.

You testified that Nucynta competes in the long acting opioid market, correct, Nucynta ER?

A. Correct, the CII long acting opioid market.

Q. In that market isn't it true that Nucynta ER, the long acting opioid, only has 1 to 2 percent of that share, of that market?

A. It's, yeah, it's, I think, in the material here. It's about 1.77 percent.

Q. If you look at the IR product, that also has less than two percent of the sales. Is that correct?

A. That's correct. They are very large markets.

Q. And you said one of the things that attracted you, attracted Depomed to the product was the DPN indication or the dual mechanism of action?

A. Dual mechanism, yes.

Q. Prior to your deposition, did you have a conversation with Dr. Vellturo?

A. Yes.

Q. And he is one of the commercial success experts for plaintiff?

A. Correct.

Q. And did you talk to him for a couple of hours?
A. About a couple of hours.
Q. And you described to him the financial forecast calculations that you did?
A. Yes.
Q. And the net present value calculations that you did?
A. Yes.
Q. Now, during that conversation, is it true that you didn't give him any information regarding the share of Nucynta ER prescriptions that are attributable to DPN diabetic peripheral neuropathy?
A. I don't recall what we physically gave him if anything.
Q. Okay. In terms of --
A. In terms of documents.
Q. Is it true that at your deposition less than two weeks ago, Depomed didn't have any knowledge regarding the percentage of its portions of sales that are attributable to DPN?
A. As far as I know I don't have that information.
Q. Depomed doesn't have that information?
A. I can't necessarily speak to everybody at Depomed but I'm not familiar with that information.
Q. Okay.
MR. PATEL: I don't believe I have any further questions but I leave it to defendants.
Thank you, Mr. Anders.

THE COURT: Thank you. Anyone else from the defendants?

MR. CAPUANO: No questions.

THE COURT: No? All right.

Any redirect from the plaintiff?

MR. SITZMAN: Let me, real quickly.

THE COURT: Do you want to take a minute?

MR. SITZMAN: Could I take a minute?

THE COURT: Yes, sure.

MR. SITZMAN: Your Honor, we don't have any further questions at this time.

THE COURT: All right. Very well.

MR. SITZMAN: Thanks.

THE COURT: You may step down. Thank you very much.

(Whereupon the witness was excused)

THE COURT: Will that be it today for witnesses or do you have someone else that you'd like? You probably have a half hour if you would like to do something with that.

MR. SITZMAN: I don't think that --

THE COURT: It's productive to start in on someone.

MR. SITZMAN: I mean it's, we certainly can't get through his direct. It will be Dr. Buschmann. And so I think if we can start in the morning and everybody --

THE COURT: We will start tomorrow morning and hopefully there are no other issues and we will start at 9:30, which is what I expect. So, we will start with that witness, Dr. Buschmann. We will work, as I say, throughout the day because I have canceled my other arrangements for the day. So, I will have the whole day here with you folks.

And I am happy to stay late, probably around 6:30, if you need to. It sounds like you may in fact need that. And barring any unforeseen events, I mean that should be the schedule that we take.

Does anyone anticipate anything else for tomorrow? Anything?

MR. ALY: Not for tomorrow. I have a housekeeping issue for today. The parties had agreed to exchange objections to exhibits disclosed by 6 p.m., assuming the Court would be done at 4:30. We just want to make it clear that we --

THE COURT: You are going to do that now.

MR. ALY: And we can talk about it now but submit --

THE COURT: That sounds fine.

MR. SITZMAN: We will accept the objection but there won't be any so --

(Laughter).

THE COURT: That should conclude it for today. Thanks so much for your time and attention today. I will see

you tomorrow morning at 9:30. We will try and get the air conditioning to work in here anyway. Enjoy the day. Thank you very much.

(Whereupon the was concluded)